Postgraduate Medicine

Volume 27 · Number 6

JUNE · 1960

OFFICIAL JOURNAL OF THE INTERSTATE POSTGRADUATE MEDICAL ASSOCIATION

TABLE *of* CONTENTS

Carcinoma of the Stomach
SAMUEL F. MARSHALL, M.D. 683

The Clinical Usefulness of Orally Administered Hypoglycemic Agents
GEORGE J. HAMWI, M.D. AND THOMAS G. SKILLMAN, M.D. 687

Rectal Impalement
ERIC F. ROUTLEY, M.D. 696

Plastic Surgical Conditions in Infancy and Childhood
KENNETH PICKRELL, M.D., NICHOLAS GEORGIADE, M.D.,
FRANK MORRIS, M.D. AND JEROME ADAMSON, M.D. 704

Drugs Most Effective in the Control of Epilepsy
FRANCIS M. FORSTER, M.D. 711

Pelvic Pain in Women
WILLIAM F. MENGERT, M.D. 716

The Use of Respiratory Stimulants
JOHN ADRIANI, M.D. 723

The Doctor's Dilemma
I. S. RAVDIN, M.D. 802

SYMPOSIUM

Treatment of Multiple Injuries Associated With Automobile Accidents
GEORGE J. CURRY, M.D., ERIC OLDBERG, M.D.,
WILSON WEISEL, M.D. AND JOHN L. KEELEY, M.D. 730

(Continued on page A-4)

Postgraduate Medicine is published monthly at Minneapolis, Minn., by IPMA Publishing Co., G. Victor Lowrie, executive vice-president; William H. Hull, professional relations manager; Muriel D. Ries, circulation manager; Fred Couzens, Eastern manager, 420 Lexington Ave., New York 17, N.Y., telephone Murray Hill 4-7752; Arthur G. Sullivan, Jr., Central-West manager, 203 North Cedar Street, Horicon, Wis., telephone Hunter 5-2003. Advertising representatives: McDonald-Thompson, 1008 Western Ave., Seattle 1, Wash.; 625 Market St., San Francisco 5, Calif.; 3727 W. 6th St., Los Angeles 5, Calif.; 2727 Oak Lane Ave., Dallas 19, Tex.; 3217 Montrose Blvd., Houston 6, Tex.; 620 Sherman St., Denver 3, Colo. Publication date: 10th of the month. Subscription rate $10.00 a year in the United States and Canada; $12.00 in foreign countries. Two volumes a year. Address all editorial and business correspondence to **Postgraduate Medicine**, Essex Building, Minneapolis 3, Minn., telephone Federal 9-8836.

© 1960 by IPMA Publishing Co.
Title Reg. U. S. Pat. Off. Second-class postage paid at Minneapolis, Minnesota and at additional mailing offices. Printed in U.S.A.

CASE REPORT

Arrhenoblastoma of the Ovary
GILLES BELISLE, M.D. AND FRANCOIS ROY, M.D. 746

CLINICAL STUDY

Diuretic Evaluation of Chlorazinal
MORTON FUCHS, M.D., WILLIAM WILSON, M.D.,
SANFORD R. MALLIN, M.D. AND LETICIA HERNANDO, M.D. 750

SCIENTIFIC EXHIBIT

Facial Pain
ARNOLD P. FRIEDMAN, M.D., CHARLES A. CARTON, M.D.
AND ASAO HIRANO, M.D. 756

CLINICOPATHOLOGIC CONFERENCE

Case Report
FROM THE VETERANS ADMINISTRATION HOSPITAL, HINES, ILLINOIS 776

NUTRITION IN CLINICAL MEDICINE

Protein Economy in the Growing Child
L. EMMETT HOLT, JR., M.D. 783

SELF-HELP DEVICES

Aids to Telephoning
EDWARD W. LOWMAN, M.D. AND HOWARD A. RUSK, M.D. 799

POSTGRADUATE CLINICAL NOTES

141. Purpose of Yawning 695
142. Myocardial Infarction 729
143. Cesarean Section 749
144. Discogenic Disease 782

DEPARTMENTS

EDITORIALS 806
What's Happening to Our Ward Rounds?
The Hospital's Fight for Survival

(Continued on page A-6)

add to her
HAPPY
ANTICIPATION

EN-CEBRIN™

(prenatal vitamin-mineral supplements, Lilly)

concentrated nutritional support

En-Cebrin provides phosphorus-free calcium . . . all known antianemia factors . . . plus important vitamins and minerals.

one-a-day convenience and economy

A single Pulvule® daily provides comprehensive vitamin-mineral supplementation throughout pregnancy and lactation.

invitingly styled

The pink-and-blue En-Cebrin Pulvules are supplied in decorative apothecary-type bottles, fashioned to enlist patient co-operation.

In special bottles of 100; also available in quantities of 5,000.

ELI LILLY AND COMPANY • INDIANAPOLIS 6, INDIANA, U.S.A.

012007

INDEX TO VOLUME 27 809

FORTHCOMING FEATURES A-9

YOUR QUESTIONS ANSWERED A-18

Immunity Against Poliomyelitis
Swollen, Hyperemic Vocal Cords
Tests for Syphilis
Probable Cerebral Atherosclerosis

WHAT'S HAPPENING IN MEDICINE ..... Facing A-32

LABORATORY NOTES A-40

New Light on the Chromosomes of Man
ELLIS S. BENSON, M.D.

FORENSIC MEDICINE A-52

Legal Ramifications of Athletic Injuries
WILLIAM N. HARSHA, M.D.
Book Review: The Medical Sourcebook
Reviewed by OLIVER SCHROEDER, LL.B.

MEETINGS AND POSTGRADUATE COURSES A-46, A-61

RADIOLOGY FOR PRACTICING PHYSICIANS A-73

Sarcoidosis
PAUL C. HODGES, M.D.

MEDICINE FROM ABROAD A-86

NEW FOR YOUR ARMAMENTARIUM A-128

PRODUCTS BY THERAPY INDICATIONS A-134

FINANCIAL PLANNING FOR THE MEDICAL PRACTITIONER
J. K. Lasser Institute ..... Facing A-164

THE MEDICAL BOOKMAN A-172

DR. PEPYS' PAGES. Morris Fishbein, M.D. A-188

THE MEDICAL MUSE. Richard Armour A-196

INDEX TO TECHNICAL EXHIBITS A-210

New (2nd) Edition – Just Ready!

Frederick and Towner – THE OFFICE ASSISTANT in Medical Practice

Packed with up-to-date help for your "Girl Friday"

You'll save yourself a vast amount of time and build up patient good will to a surprising degree if you present your office assistant with a copy of this little book. Whether she's a "new girl" or a faithful "right arm" who's been with you for years—she'll find 100's of useful tips here. The book is packed with help on every phase of her job—as receptionist, secretary, bookkeeper, nurse and technician. The authors have brought this *New (2nd) Edition* right up to the minute. The chapter on Bookkeeping has been greatly expanded with many new illustrations of up-to-date office forms, a description of the "write-it-once" bookkeeping system, etc. The chapter on Instruments is now much more detailed and clearly illustrated and includes new help on sterilization.

By Portia M. Frederick, Instructor, Medical Office Assisting, Long Beach City College; and Carol Towner, Director of Special Services, Communications Division, American Medical Association. About 400 pages, 5¼" x 8", illustrated. About $5.25. *New (2nd) Edition—Just Ready!*

The New MAYO CLINIC Volume

Always a favorite with both general practitioners and specialists, the latest Mayo Clinic Volume is just off press. It brings you the first-hand report of the medical and surgical advances made during 1959 at this world-famous center. 137 articles offer new help on such problems as: appraisal of kidney function tests—the irritable colon syndrome—hormone therapy in obstetrics and gynecology—role of the family physician in treatment of children with congenital heart disease—sprains, strains and whiplash injuries—management of emotional stress in the housewife—surgical treatment of endocardial cushion defects, etc. Order your copy of this useful volume today. *The edition is limited and the book will not be reprinted.*

Collected Papers of The Mayo Clinic and Mayo Foundation. Volume 51. By The Staff of the Mayo Clinic, Rochester, Minnesota; and The Mayo Foundation, University of Minnesota. About 864 pages, 6" x 9", with 246 illustrations. $14.00 *Papers of 1959—Just Ready!*

NEW! – Mulholland, Ellison & Friesen – Current Surgical Management II

This stimulating new book (the second in the Surgical Management Series) brings you varying viewpoints of eminent surgeons on 16 controversial surgical diseases. An authority closely identified with each of the different procedures (Drs. Wangensteen, Cattell, Colcock, Braasch, Haagensen, etc.) explains the "how" and "why" of the treatment he prefers. Differing approaches in widest use are given for management of: duodenal ulcers; polyps of the colon; carcinoma of the pancreas; common duct stricture; pilonidal sinus; acute renal failure; thromboembolism; etc.

Edited by John H. Mulholland, M.D., George David Stewart Professor of Surgery, New York University College of Medicine; Edwin H. Ellison, M.D., Professor and Chairman of the Department of Surgery, Marquette University School of Medicine; and Stanley R. Friesen, M.D., Associate Professor of Surgery, Pathology and Oncology, University of Kansas School of Medicine. With contributions by 50 American Authorities. About 334 pages, 6¼" x 9¾", illustrated. About $8.00. *New—Just Ready!*

ORDER TODAY!

W. B. **SAUNDERS** Company, West Washington Square, Philadelphia 5 PGM 6-60

Please send me the following books and charge my account:

- ☐ *Frederick and Towner's Office Assistant* ..... *About $5.25*
- ☐ *The New Mayo Clinic Volume* *$14.00*
- ☐ *Mulholland et al.—Current Surgical Management II* ..... *About $8.00*

Name _____

Address _____

Your Questions answered

Readers may send questions from their own practice or other medical problems which will be answered by qualified consultants. Replies are forwarded by mail immediately and selected questions and answers are published each month in this section.

• IMMUNITY AGAINST POLIOMYELITIS

Q. What is the duration of immunity following the usual course of three injections of Salk vaccine? I am constantly being asked how frequently booster injections should be given, and I can find no authoritative information on this subject.

I would also appreciate references to any statistics on the effectiveness of the vaccine in any epidemics which have occurred since its use.

M.D.—Quebec

A. Last year, at the request of Surgeon General Leroy E. Burney of the United States Public Health Service, an advisory committee made the following recommendations on the dosage and schedules for poliomyelitis vaccination. All persons less than 40 years of age should receive four doses of 1 ml. each. For infants aged two to six months, the first three doses should be spaced one month apart, and the fourth dose should be administered 7 to 12 months after the third. For all other persons, the second dose should be given four to six weeks after the first, the third 7 to 12 months after the second, and the fourth a year or more after the third. Further information can be found in the *Journal of the American Medical Association* (170:27 [July 11] 1959).

The committee made no recommendations for routine booster doses following the fourth injection. Available data are inadequate to show whether or not supplementary booster doses are needed.

It is difficult to analyze available data on epidemics. In the majority of cases, paralytic poliomyelitis occurred in persons who had not been vaccinated or who had had one or two doses. This was the experience in the 1958 epidemics in Detroit and Winnipeg. However, only a rough estimate can usually be made concerning the number and age distribution of vaccinated and unvaccinated patients. It is even more difficult to evaluate the effectiveness of vaccination campaigns initiated while an epidemic is in progress.

Additional information on the Detroit and Winnipeg epidemics can be found in the *Journal of the American Medical Association* (169:1838-1842 [April 18] 1959) and in the *Canadian Medical Association Journal* (80:436-439 [March 15] 1959).

• SWOLLEN, HYPEREMIC VOCAL CORDS

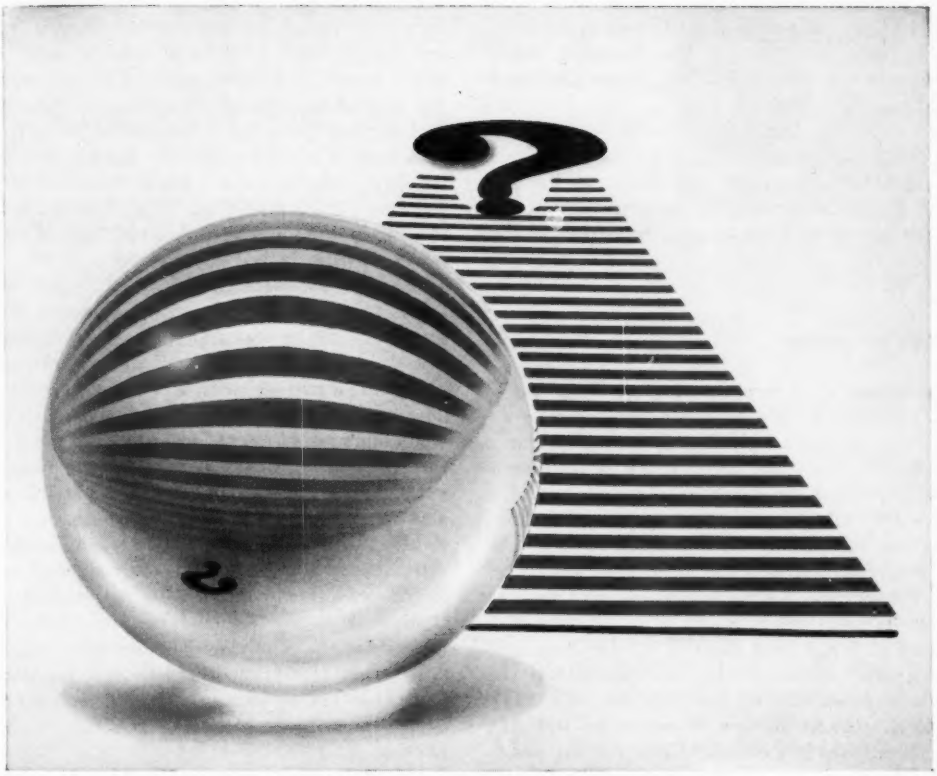
Q. In 1956, a 42 year old man had acute laryngitis with almost complete loss of voice. Marked improvement occurred following a period of voice rest, and the patient was more or less asymptomatic until July 1959. At that time, hoarseness recurred and was accompanied by discomfort in the region of the larynx. There were no abnormal physical findings.

On examination both vocal cords were swollen and hyperemic. The pathologic report of a biopsy of tissue taken from both cords was leukoplakia. Is this condition a precursor to cancer when found on the vocal cords, or can it be associated with benign lesions and chronic laryngitis? What treatment is indicated?

M.D.—British Columbia

A. Leukoplakia on the vocal cords can be considered a precursor to cancer. In general, the

(Continued on page A-20)



what lurks beyond the broad spectrum?

Broad spectrum antibiotics provide the best means of combating pathogenic organisms which range all the way from large protozoa through gram-negative and gram-positive bacteria to certain viruses at the far end of the spectrum.

But beyond the spectrum lurk pathogenic fungi. It is increasingly apparent that fungal superinfections may occur during or after a course of broad spectrum antibiotics.[1,2] Long term debilitating diseases, diabetes, pregnancy, corticosteroid therapy, high or prolonged antibiotic dosage, and other causes may predispose to fungal superinfections.[1,3,4]

Mysteclin-V controls infection and prevents superinfection. It makes a telling assault on bacterial infections and, in addition, prevents monilial overgrowth.[2,5-8] Mysteclin-V is a combination of tetracycline phosphate complex for reliable control of most infections encountered in daily practice, and Mycostatin, the safe antifungal antibiotic. When you prescribe Mysteclin-V, you provide "broad spectrum therapy" plus extra protection that extends beyond the spectrum of ordinary antibiotics.

In pediatrics: Mysteclin-F for Aqueous Drops and Mysteclin-F for Syrup are phosphate-potentiated tetracycline combined with the new antifungal antibiotic, Fungizone (amphotericin B). They provide good-tasting, fruit-flavored aqueous liquids for your pediatric patients.

Supplied: Mysteclin-V Capsules (250 mg./250,000 u.); Half-strength Capsules (125 mg./125,000 u.); Mysteclin-F for Syrup (125 mg./25 mg. per 5 cc.); for Aqueous Drops (100 mg./20 mg. per cc.)

References: 1. Dowling, H. F.: Postgrad. Med. *23*:594 (June) 1958. 2. Gimble, A. I.; Shea, J. G., and Katz, S.: Antibiotics Annual 1955-1956 New York, Medical Encyclopedia Inc., 1956, p. 676. 3. Long, P. H., in Kneeland, Y., Jr., and Wortis, S. B.: Bull. New York Acad. Med. *33*:552 (Aug.) 1957. 4. Rein, C. R.; Lewis, L. A., and Dick, L. A.: Antibiotic Med. & Clin. Ther. *4*:771 (Dec.) 1957. 5. Stone, M. L., and Mersheimer, W. L.: Antibiotics Annual 1955-1956, New York, Medical Encyclopedia Inc., 1956, p. 862. 6. Campbell, E. A.; Prigot, A., and Dorsey, G. M.: Antibiotic Med. & Clin. Ther. *4*:817 (Dec.) 1957. 7. Chamberlain, C.; Burros, H. M., and Borromeo, V.: Antibiotic Med. & Clin. Ther. *5*:521 (Aug.) 1958. 8. From, P., and Alli, J. H.: Antibiotic Med. & Clin. Ther. *5*:639 (Nov.) 1958.

Mysteclin-V

Tetracycline Phosphate Complex (Sumycin) and Nystatin (Mycostatin)

SQUIBB *Squibb Quality—the Priceless Ingredient*

'MYSTECLIN'®, 'SUMYCIN'®, 'MYCOSTATIN'®, AND 'FUNGIZONE'® ARE SQUIBB TRADEMARKS.

lesion should be removed if the clinical setting will permit it. However, the gross description of this patient's condition leads to the suspicion that he has some polypoid thickening of the vocal cords rather than leukoplakia. In itself, leukoplakia does not cause swollen, hyperemic vocal cords.

This patient should be followed very closely, and repeated examinations of the larynx should be made to ascertain the true nature of the disease. Treatment depends on the pathologic status of the larynx and the general condition of the patient.

• TESTS FOR SYPHILIS

Q. A man died recently of a syphilitic aneurysm which had been discovered a year or so ago. He had had no previous history of primary or secondary disease, and the last Wassermann test, in 1945 or 1946, had given negative results. The only contact that could have caused the disease was believed to have occurred in 1942. At the time the aneurysm was discovered, results of the Wassermann test were positive, and the patient was given penicillin.

This man had been married for 15 years and had several children. His wife would like to know whether she or the children may have syphilis. Results of her Wassermann test are negative. Does this definitely rule out the possibility that she may have syphilis?

M.D.—North Dakota

A. Negative results of the Wassermann test serve as a very important guide in helping us to rule out the presence of syphilis. However, at many of the centers at which the various titers of complement-fixation tests are studied, it has been concluded that the TPI test (*Treponema pallidum* immobilization) is almost a specific test for syphilis. More recently, the TPCF test (*T. pallidum* complement fixation) has been developed and has given results which are closer to being 100 per cent accurate than are the results of the TPI test. A comparison of results of the two tests shows an 87.3 per cent agreement.

• PROBABLE CEREBRAL ATHEROSCLEROSIS

Q. A 62 year old woman has Meniere's syndrome, but for a long period the attacks of vertigo were prevented by adequate treatment. Recently, however, in the midst of a conversation she had a lapse of memory and fell while attempting to reach her bed. She felt slightly dizzy, but did not have a headache or chest pain. The attack lasted 10 minutes, and she then recovered her mental faculties. A cardiologist was called, and she was given an antihistamine. A physical examination yielded essentially normal findings; her only complaint was a slight numbness of the left arm, but her grip was normal. The attack was diagnosed as a vascular episode, and she was advised to stay in bed the next day.

About one hour after the attack, rales developed at the base of the right lung, and 1/6 gr. of morphine sulfate was administered by hypodermic injection to control apparent pulmonary edema. The patient slept well during the night. The next day an electrocardiogram was taken, and a diagnosis of acute anterior myocardial infarct was made. She was taken to the hospital, where she was given oxygen (5 l. per minute) and complete bed rest was prescribed. She also received DEPO-HEPARIN® sodium, administered intramuscularly, and 100 mg. DICUMAROL® each day. Tests were conducted daily to determine the prothrombin, bleeding and clotting times. The administration of oxygen has now been stopped, and she is receiving only 100 mg. Dicumarol daily. She has no paralysis, buccal deviation or edema but is affected by meteorism and occasional constipation.

Physically, the patient seems to be progressing satisfactorily, but she still has symptoms of a mental disturbance. She cannot yet remember key events of her daily life, although she can follow a conversation quite well. What underlying condition would produce this mental disturbance and what treatment should be carried out to bring about improvement? Also, what should be done to prevent the occurrence of another infarct?

M.D.—Puerto Rico

A. The most likely underlying cause is cerebral atherosclerosis. It seems altogether possible that there may be an infarct in the right frontal region, and of course there may be any number of silent infarcts which have occurred at some other time in the past. As far as amelioration of these symptoms is concerned, the only treatment is rehabilitation and retraining of some of the lost talents. In certain instances similar to this, the long-term use of anticoagulants has been advised to prevent additional occurrences.

What's happening in Medicine

POSTGRADUATE MEDICINE'S REPORT of late news of interest to practicing physicians

FIVE YEAR STUDY OF CORTICOSTEROIDS

The American College of Physicians:

- Use of corticosteroid drugs for five years or more in 190 patients with rheumatoid arthritis has shown that anatomic deformity of joints continues despite preservation of functional capacity. An attempt to gain more function and possibly to lessen joint destruction by increasing the dosage of corticosteroids was found unwise. Hopes of avoiding undesirable effects of treatment by using partially suppressive dosage have not been realized. Six deaths were attributed to corticosteroids and six additional fatalities may have been due in part to their use. Almost all patients had one or more undesirable changes in appearance.—Drs. Carl A. Berntsen, Jr. and Richard H. Freyberg, Cornell University Medical College, New York.

- Use of traumatic catheterization and angiocardiography in evaluating rheumatic heart lesions can be avoided by employing combinations of phonocardiography; three-plane ballistocardiography; records of jugular, carotid and apical pulsation, and slit kymography. In some cases these have proved more revealing than have catheter studies plus angiocardiography. They also are of value in patent ductus arteriosus and pulmonary stenosis, but not in locating shunts or anomalous venous return.—Dr. William Dock, State University of New York College of Medicine, Brooklyn.

- Studies offer no indication that aldosterone hypersecretion participates in the pathogenesis of primary (essential) hypertension. But the data do establish that the syndrome of malignant hypertension usually is associated with such hypersecretion.—Dr. John H. Laragh and associates, Columbia University College of Physicians and Surgeons, New York.

TWENTY-FOUR HOUR STREPTOCOCCUS TEST

Society of American Bacteriologists:

- Streptococci in throat cultures can be identified within 24 hours by a method known as inhibition of common antigen fluorescence. To observe the fluorescence, the specimen must be viewed under a beam of ultraviolet light. Practical application of this method in identifying group A streptococci previously had been complicated by the fact that several types of organisms, including staphylococci, have the same fluorescent appearance. The current method uses a culture medium in which staphylococci will not multiply and in which a nonfluorescent agent is used to prevent the reaction of streptococci other than group A, which may be a forerunner of rheumatic fever.—Earle K. Borman, Connecticut State Department of Health, Hartford.

Seborrheic dermatitis in infants

American Academy of Pediatrics:

• Evidence is becoming more convincing that seborrheic dermatitis in infants is due to a biotin deficiency. Biotin, previously called vitamin H, is found mostly in liver, egg yolk, yeast and kidneys. Biotin in food is not utilized by some infants, perhaps because of inability to break down its peptide linkage to protein. When the nursing mother is fed liver or is given biotin injections, the biotin excreted in the breast milk will clear up seborrhea in the infant. Inadequate biotin in the diet of the nursing mother produces seborrhea. Synthetic biotin given orally and by injection has improved a large number of infants. A significant finding in infants with seborrheic dermatitis is a bright, diffuse erythema over the perineum.—Dr. Aaron Nisenson, Children's Hospital, Los Angeles.

Cardiovascular effects of nicotine

Cardiovascular Conference, New York Academy of Sciences:

• In patients with coronary artery disease, cigarette smoking increased the pulse rate, systemic arterial pressure and cardiac output. As a result of these changes, the ratio of work to oxygen consumption increased. These data suggest that the anginal pain experienced by some individuals during smoking may be the result of increased work of the heart rather than of diminution in coronary blood flow.—Dr. Timothy J. Regan, Wayne State University College of Medicine, Detroit.

Fibrinolysis in thrombosis

Symposium on fibrinolysis, Sloan-Kettering Institute, New York:

• Of 45 patients with coronary thrombosis who were treated with fibrinolysin, 39 are still living. Significant side reactions were noted in only four patients; all showed evidence of bleeding. Results of treatment depend on a number of variables, the most important of which are size and location of the involved vessel. Others are age of patient, state of general circulation, degree of pain, presence of shock and congestive heart failure, and promptness of initiating fibrinolytic therapy. In this series, 11 patients were treated in three to five hours after the onset of an appreciable degree of pain; 20 in 6 to 10 hours, and the remainder in 11 to 120 hours.—Dr. Isaac H. Richter, Coney Island Hospital, Brooklyn.

• Fifty patients admitted to the hospital with thrombophlebitis were treated with fibrinolysin, anticoagulants and bed rest. Pain disappeared in an average of 3.8 days and the size of the leg was reduced in 3.3 days. In a comparable series reported by another investigator in which the patients were treated with anticoagulants and bed rest alone, resolution of pain required 8.1 days and reduction in size of the extremity 7.2 days.—Dr. Nancy D. Davis, Muhlenberg Hospital, Plainfield, N. J.

Influenza protection extended

International Conference on Asian Influenza:

• Significant antibody levels have been found three years after administration of polyvalent flu vaccine with a mineral oil adjuvant. It seems reasonable to state that we have in the adjuvant a device to obviate annual vaccination. Data also suggest that polyvalent vaccine will provide significant protection in most outbreaks of influenza even though it does not contain the specific mutant strain involved.—Dr. Fred M. Davenport, University of Michigan Medical School, Ann Arbor.

ALPEN is the oral penicillin that provides, on a fasting stomach, peak antibiotic blood levels approximately twice as high as oral potassium penicillin V... and significantly higher than I. M. penicillin G.

Some strains of staphylococci resistant to other penicillins exhibit in vitro sensitivity to potassium phenethicillin.

ALPEN has greater freedom from the G. I. sequelae (overgrowth of resistant flora) sometimes observed with broad spectrum -mycins.

ALPEN gives much higher antibiotic levels within the first hour of ingestion by the well-tolerated oral route.

WHEN TO USE ALPEN Recommended in the treatment of infections caused by pneumococci, streptococci, gonococci, corynebacteria, and penicillin-sensitive staphylococci.

HOW TO USE ALPEN Depending on the severity of the infection, 125 mg. (200,000 units) or 250 mg. (400,000 units) three times daily may be used. In more severe or stubborn infections, a dosage of 500 mg. (800,000 units) t.i.d. may be employed. In beta hemolytic streptococcal infections, treatment should be continued for at least ten days.

PRECAUTIONS The usual precautions in the administration of oral penicillin should be observed. For further details see package literature.

Tablets: 125 mg. and 250 mg., bottles of 25 and 100. Powder for Oral Solution (lemon-lime flavored), 1.5 Gm. bottle (125 mg. per 5 cc. teaspoonful).

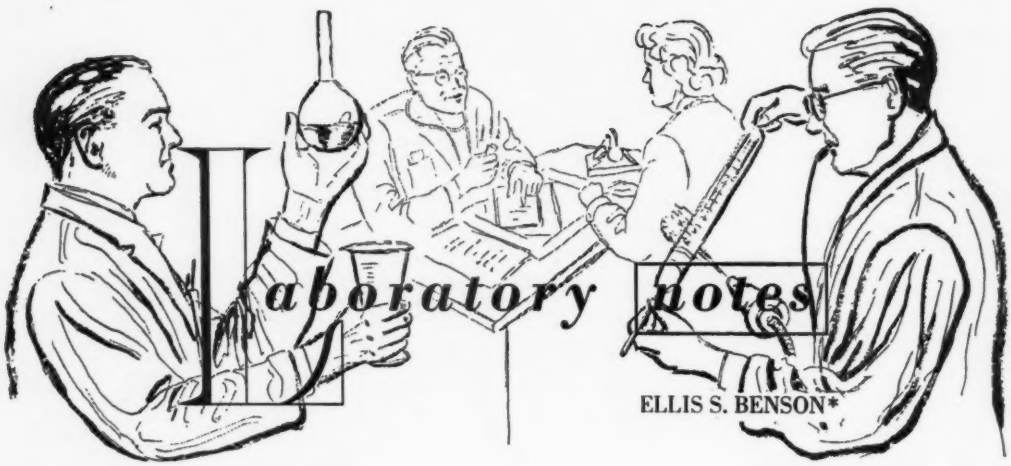
this is the tablet that gives higher peak antibiotic blood levels

HIGHER THAN I. M. PENICILLIN G
HIGHER THAN POTASSIUM PENICILLIN V

ALPEN

ALPEN™—potassium phenethicillin

Schering



ELLIS S. BENSON*

New Light on the Chromosomes of Man

In 1949, Barr and Bertram[1] observed a special mass of chromatin in the nucleus of epidermal cells near the inner surface of the nuclear membrane. This mass has characteristics which distinguish it from other chromatin particles, notably its greater size, its planoconvex shape, and its location against the nuclear membrane. The presence of this chromatin mass took on great importance because it was observed in the cells of females but not in those of males. It became known as the "sex chromatin mass."

The sex chromatin mass was thought to represent in some way the two X chromosomes of the female and the absence of it in males, or its presence in only a very small number of male cells, the result of the XY sex chromosome combination in males. This seemed a reasonable assumption, and since this discovery offered a practical method for assessing sex chromosome constitution, it led to the study of sexual anomalies in man, such as Turner's syndrome and Klinefelter's syndrome.

Turner's syndrome, or ovarian agenesis, occurs in individuals who are apparently females. These individuals characteristically show sexual infantilism, are female in type and of short stature, and have a high urinary excretion of gonadotropins. Other congenital abnormalities are frequently associated, most notably webbed neck, an increased carrying angle of the arm, skeletal abnormalities, and coarctation of the aorta. Many investigators, including Grumbach, Van Wyk and Wilkins,[2] found that in this condition the great majority of affected individuals had epithelial cells which lacked the sex chromatin mass and thus had a "male" sex chromatin pattern.

Conversely, in studying patients with testicular disorders, the sex chromatin pattern was found to be "female" in type in many who fell into the classification of Klinefelter's syn-

(Continued on page A-42)

*Director of Hospital Laboratories and Associate Professor of Clinical Laboratory Medicine and of Pathology, University of Minnesota Medical School, Minneapolis, Minnesota.

by ORAL administration

"knock the stuffings" out of nasal stuffiness due to sinusitis—with

Naldecon™

The long-acting nasal decongestant with the therapeutic "one-two"

Superior relief of nasal stuffiness due to sinusitis, through a unique "counterbalanced" formula of four ingredients—two decongestants and two antihistaminics. Round-the-clock benefits on only three tablets a day.

Each long-acting NALDECON "tablet-within-a-tablet" contains:

	Outer Layer (3 to 4 hours relief)	Inner Core (additional 3 to 4 hours relief)	Total Content (6 to 8 hours relief)
Decongestants:			
Phenylephrine HCl	5 mg.	5 mg.	10 mg.
Phenylpropanolamine HCl	20 mg.	20 mg.	40 mg.
Antihistaminics:			
Phenyltoloxamine citrate	7.5 mg.	7.5 mg.	15 mg.
Chlorpheniramine maleate	2.5 mg.	2.5 mg.	5 mg.

Each teaspoonful (5 cc.) of NALDECON Syrup contains the equivalent of one-half a NALDECON Tablet.

SUPPLY: Tablets, scored, bottles of 50. Syrup, prescription bottles of 16 oz.

BRISTOL LABORATORIES, SYRACUSE, N. Y.

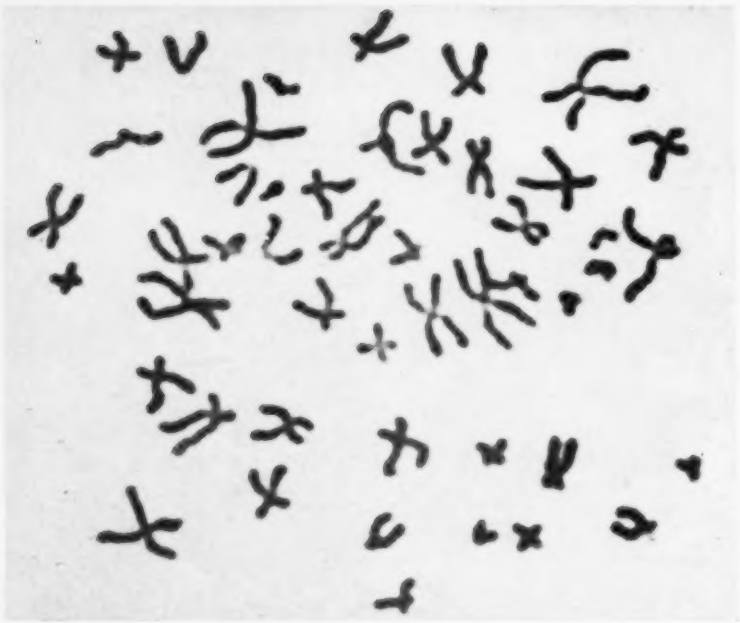


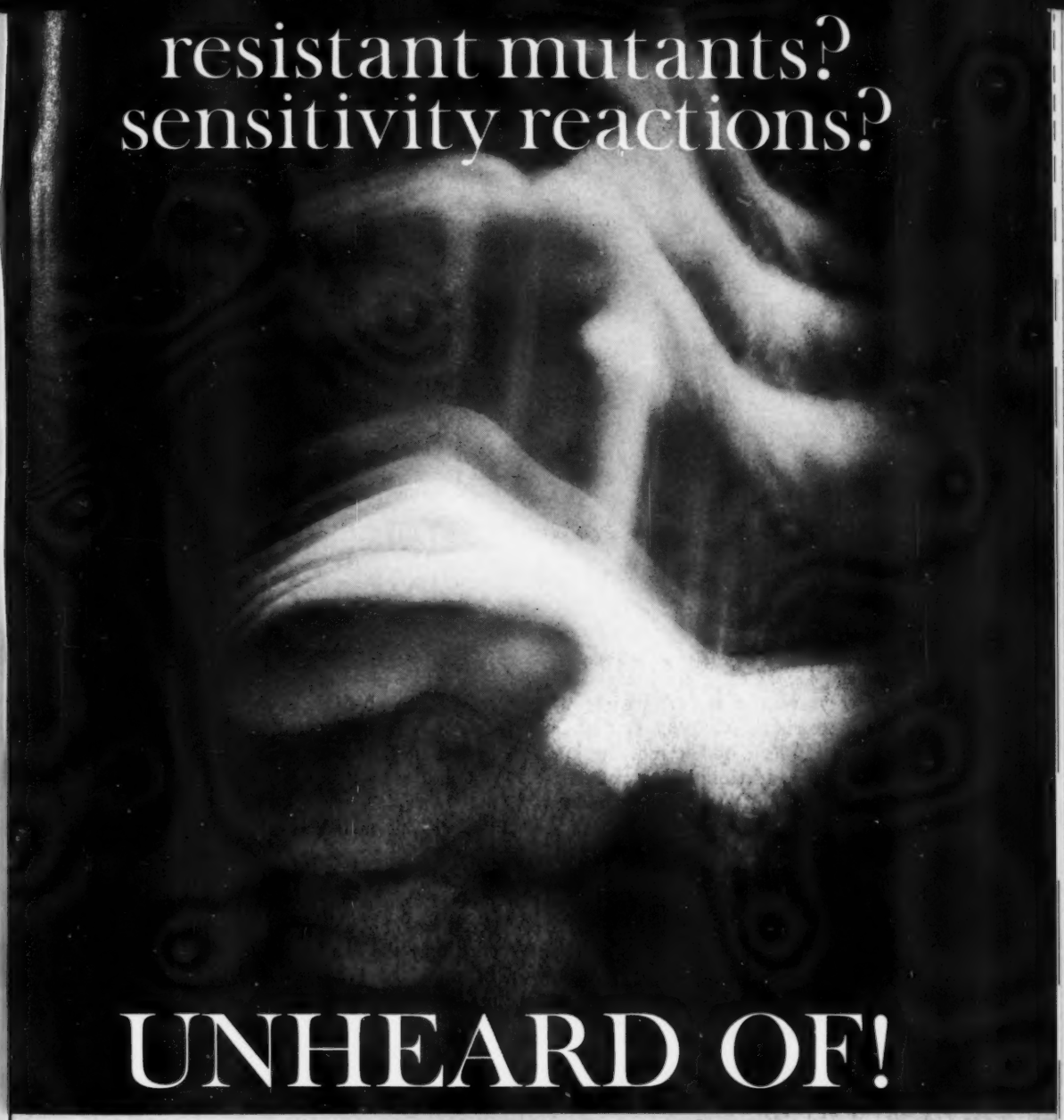
FIGURE 1. Mitotic metaphase arising in a bone marrow cell.

drome.[3] Klinefelter's syndrome occurs in persons who are apparently male and who have the combination of testicular atrophy and failure of development of the seminiferous tubules, gynecomastia and high urinary excretion of gonadotropins.

A consideration of these findings and of the gene theory as it applies to sexual development led naturally to the suggestion that the patients with Turner's syndrome were genetically male and had an XY chromosome complex. Similarly those individuals with Klinefelter's syndrome who show a "female" sex chromatin pattern are in fact "genetic females," with XX complex. The influences which resulted in a "genetic male" developing female habitus and a "genetic female" developing male habitus were thought to be extragenetic. These conclusions were based on the assumption that there were only two types of sex chromosome complex, XX and XY.

In 1959, a series of very important and exciting reports began to appear. These reports dealt with the first fruits of a technical advance which may revolutionize human genetics and which already has cast new light on the significance of the discrepancies between sex chromatin and body habitus in the sexual anomalies mentioned before. Technical accomplishments painstakingly accumulated over a number of years finally made it possible to study human chromosomes by direct cytologic technics.[4] In these technics, a "squash" preparation of bone marrow cells was used, swollen by hypotonic saline and fixed in the metaphase of mitosis by use of colchicine (figure 1). The first triumph of the new technics occurred in 1956 when it was demonstrated that man possessed only 46 individual chromosomes,[5] rather than the long-believed 48. Then, in 1959, Jacobs and Strong,[6] using these new technics of Ford and his collaborators,[4] found in a case of Klinefelter's syndrome that bone marrow cells contained not 46 but 47 chromosomes, and in pairing these the extra chromosome appeared to be an X chromosome, making the sex chromosome XXY. In a case of Turner's syndrome (gonadal dysgenesis), 45 chromosomes were found.[7] A sex chromosome was the missing one, giving an unpaired (haploid) XO chromosome pattern rather than the

(Continued on page A-44)



in urologic patients taking

MANDELAMINE®

brand of methenamine mandelate

This is why Mandelamine is so excellent to use in chronic resistant urinary disorders. Antibacterial but *not* antibiotic, Mandelamine is highly effective against many organisms *resistant* to antibiotics (and sulfas, too). And since Mandelamine works solely within the urinary tract, sensitivity risks and systemic reactions are relatively rare, even during prolonged usage. Mandelamine is effective, well tolerated, and economical, too.

DOSAGE: *Adults*—average dose is 2 Mandelamine Hafgrams, q.i.d. *Children over 5*—1 Mandelamine Hafgram q.i.d. *Children under 5*—1 tsp. Mandelamine Suspension q.i.d. SUPPLIED: Mandelamine Hafgrams® (0.5 Gm. tablets); 0.25 Gm. tablets; also pleasantly flavored Mandelamine Suspension containing 0.25 Gm. methenamine mandelate per 5-cc. teaspoonful.

WARNER CHILCOTT

MORRIS PLAINS, N.J.

MA-GP01

FIGURE 2. Chromosomes from a bone marrow cell of a patient showing both Klinefelter's syndrome and mongolism. The chromosomes are arranged in pairs, in order of size. The X chromosomes are seventh in order. Note the XXY combination. A supernumerary small chromosome is included with pair 23.

(Figures 1 and 2 reproduced courtesy of Dr. C. E. Ford.[10])

XY pattern previously assumed on the basis of the "nuclear sexing" technic of Barr.

Furthermore, reports[8,9] appeared indicating there was also an odd number of chromosomes in mongolism, 47, the extra one being a small supernumerary somatic one. A patient with combined Klinefelter's syndrome and mongolism was found to have 48 chromosomes, possessing both an additional X chromosome (with the complex XXY) and a supernumerary small one of mongolism[10] (figure 2).

In commenting on these findings, the editor of the *Lancet* wonders: "Is an XXY a female with an extra Y or a male with an extra X; is an XO a male with a lost Y or a female with a lost X?"[11] Obviously no answers to these questions can be given now, but it is equally obvious that the old assumptions that chromatin positivity in Klinefelter's syndrome made these individuals "genetic females" and chromatin negativity in Turner's syndrome indicated "genetic maleness" must be abandoned. The idea that the Y chromosome is inert, a useless appendage, is also no longer tenable—otherwise XXY would result in a normal female and XO in a normal male, instead of persons with Klinefelter's syndrome and Turner's syndrome, respectively.

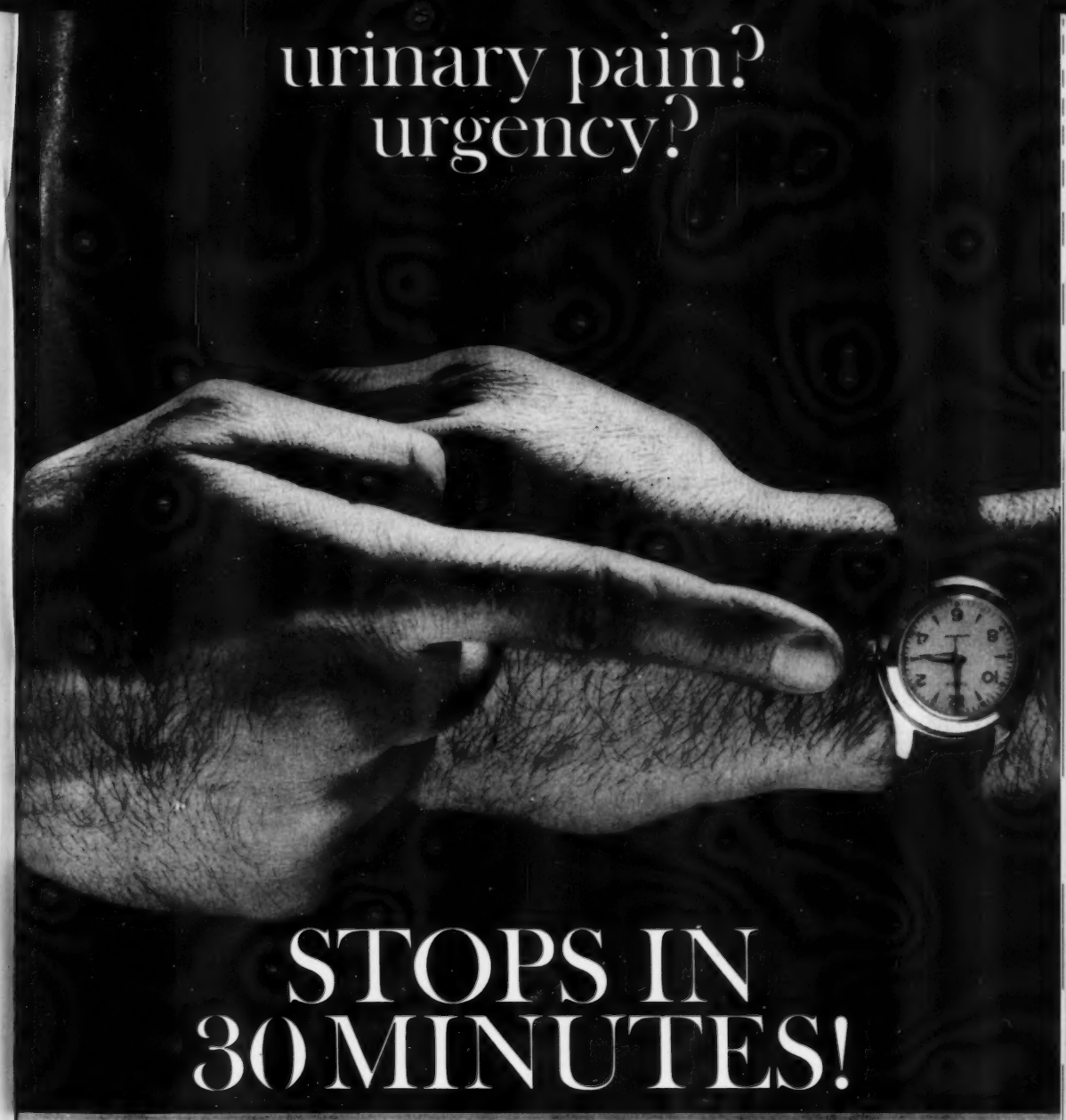
Recently a case of acute leukemia was reported[12] in which the bone marrow cells had a modal chromosome number of 48 and in which there were abnormalities of chromosome form as well, suggesting an escape in this case from normal pathways of cell differentiation. In three or four other cases of acute leukemia chromosome abnormalities were seen. This report also suggests a new and interesting avenue which these studies may take, that of proliferative abnormalities of the bone marrow.

Other sexual developmental abnormalities and other forms of mental defects and congenital abnormalities are very likely to be subjects of future study, as are the leukemias, lymphomas and other generalized neoplastic processes. But the technic of chromosome counting is not a simple one and to my knowledge only the two laboratories, at Harwell in England and Edinburgh in Scotland, are at present conducting this type of study.

On the other hand, the technic of "nuclear sexing" developed by Barr is relatively simple. It is not invalidated by the interpretations which have been made. The presence of "sex chromatin" indicates the presence of the XX complex but not necessarily genetic femaleness (since the intersex complex XXY would be possible). It is best designated as chromatin positivity. Chromatin negativity, the absence of the "sex chromatin," indicates X, that is, the presence of either the male genetic complex XY or of the intersex XO.

I have had no personal experience with the

(Continued on page 46)



STOPS IN 30 MINUTES!

after the first dose of

PYRIDIUM®

brand of phenylazo-diamino-pyridine HCl

This is why Pyridium is so desirable for urologic patients with pain, burning, frequency or urgency. Pyridium brings fast comforting relief—usually within 30 minutes—because of its *local* analgesic effect. Since Pyridium is compatible with all antibacterials, it permits more flexible therapy. Thus, you can give the agent of your choice to control any underlying infection. And unlike fixed analgesic-antibacterial combinations, Pyridium provides greater symptomatic relief in the recommended daily dose. This relief can be maintained for as long as necessary, because Pyridium is extremely well tolerated. AVERAGE DOSE: *Adults*—2 tablets t.i.d. *Children (9 to 12)*—1 tablet t.i.d. SUPPLIED: 0.1-Gm. tablets, bottles of 50, 500 and 1,000.

WARNER CHILCOTT
MORRIS PLAINS, N.J.

PY-GP01

Barr technic. Dr. E. L. Makowski[13] of the Department of Obstetrics and Gynecology, University of Minnesota, has used successfully a technic applied to buccal mucosal cells. His method is briefly as follows:

A clean slide is prepared by smearing its surface with an egg albumen-glycerin mixture.* The sample is obtained by scraping the buccal mucosa with a tongue blade. The scrapings are smeared on the prepared slide, placed immediately in a 1:1 mixture of 95 per cent ethyl alcohol and absolute ether† and fixed in this mixture at room temperature for two hours. The slide is then placed in the following solvents in series for five minutes each: 70 per cent ethyl alcohol, 50 per cent ethyl alcohol, and distilled water. It is then washed three times on each side with distilled water, and placed in a 1 per cent aqueous solution of cresylecht violet for eight minutes. Following this, it is dipped briefly (three seconds) in 95 per cent ethyl alcohol. It is placed in absolute ethyl alcohol for one minute, in xylene for five minutes, and then in a second quantity of xylene for five minutes. It is then coverslipped and is ready for examination under the oil immersion objective of the microscope. Nuclei which show pycnosis, hypochromasia and fragmentation should be excluded. Only vesicular nuclei with intact nuclear membranes are counted. The incidence of nuclear sex chromatin masses is 0 to 5 per cent of nuclei in normal males (chromatin negativity) and 20 to 80 per cent in normal females (chromatin positivity).

*Fresh egg white is mixed and filtered through gauze. To it is added an equal volume of glycerin and a few crystals of sodium salicylate.

†The 95 per cent ethyl alcohol and absolute ether should be changed frequently, preferably after each four slides.

REFERENCES

1. Barr, M. L. and Bertram, E. G.: A morphological distinction between neurones of the male and female. Nature 163:676, 1949.
2. Grumbach, M. M., Van Wyk, J. J. and Wilkins, L.: Chromosomal sex in gonadal dysgenesis; relationship to male pseudohermaphrodism and theories of human sex differentiation. J. Clin. Endocrinol. 15:1161, 1955.
3. Grumbach, M. M., Blanc, W. A. and Engle, E. T.: Sex chromatin pattern in seminiferous tubule dysgenesis and other testicular disorders; relationship to true hermaphrodism and to Klinefelter's syndrome. J. Clin. Endocrinol. 17:703, 1957.
4. Ford, C. E., Jacobs, P. A. and Lajtha, L. G.: Human somatic chromosomes. Nature 181:1565, 1958.
5. Tjio, J. H. and Levan, A.: The chromosome number of man. Hereditas 42:1, 1956.
6. Jacobs, P. A. and Strong, J. A.: A case of human intersexuality having a possible XXY sex-determining mechanism. Nature 183:302, 1959.
7. Ford, C. E., Jones, K. W., Polani, P. E., de Almeida, J. C. and Briggs, J. H.: A sex-chromosome anomaly in a case of gonadal dysgenesis (Turner's syndrome). Lancet 1:711, 1959.
8. Lejeune, L., Gauier, M. and Turpin, R.: The chromosomes of man in human culture. Compt. rend. Acad. sc. Paris 248:602, 1959.
9. Jacobs, P. A., Baikie, A. G., Court Brown, W. M. and Strong, J. A.: The somatic chromosomes in mongolism. Lancet 1:710, 1959.
10. Ford, C. E., Jones, K. W., Miller, O. J., Mittwoch, U., Penrose, L. S., Ridler, M. and Shapiro, A.: The chromosomes in a patient showing both mongolism and the Klinefelter syndrome. *Ibid.*, p. 709.
11. Editorial: The chromosomes of man. *Ibid.*, p. 715.
12. Baikie, A. G., Court Brown, W. M., Jacobs, P. A. and Milne, J. S.: Chromosome studies in human leukemia. Lancet 2:425, 1959.
13. Makowski, E. L.: Sex determination from nuclear morphology. Univ. Minnesota M. Bull. 28:190, 1957.

MEETINGS and Postgraduate Courses

Association of Military Surgeons, Washington, D.C.: The date of the annual convention, to be held at the Mayflower Hotel, has been changed to October 31-November 2. For further information, write to: Association Headquarters, 1726 Eye Street, N. W., Washington 6, D.C.

The American Institute of Oral Biology, Palm Springs, California: Seventeenth annual meeting to be held October 8-12, preceding the meeting of the American Dental Association in Los Angeles. For further information, write to: Hermann Becks, President, Board of Directors, The American Institute of Oral Biology, 2240 Channing Way, Berkeley 4.

New York University Post-Graduate Medical School, New York: Third international prosthetics course, sponsored by the International Society for the Welfare of Cripples, to be held August 15-26. Separate courses will be given for physicians and surgeons, therapists and prosthetists. For further information, write to: Dr. Sidney Fishman, Director, Prosthetics Education, New York University Post-Graduate Medical School, 342 East 26th Street, New York 10.

The University of Texas Postgraduate School of Medicine, Houston: Symposium on coronary artery disease to be held at the Texas Medical Center, November 28-December 2. For further information, write to: Office of the Dean, The University of Texas Postgraduate School of Medicine, 410 Jesse Jones Library Building, Texas Medical Center, Houston 25.

In response to physician demand

more Esidrix has been added to

SERPASIL®-ESIDRIX®

potentiated antihypertensive now available in 2 strengths

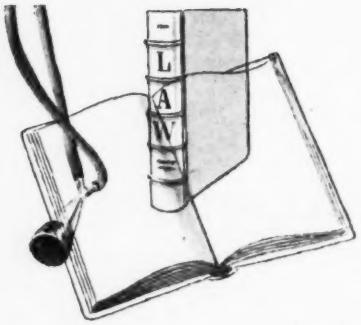
To meet the needs of patients who require greater diuretic-antihypertensive activity, Serpasil-Esidrix is now made available in a combination tablet containing **50 mg. Esidrix** and 0.1 mg. Serpasil. This tablet, Serpasil-Esidrix #2, will help you control high blood pressure in more patients. With Serpasil-Esidrix #2, you can expect a quick response: blood pressure usually begins to drop during the first few days of therapy. Excess fluid is also rapidly eliminated. And you give patients the additional benefits of Serpasil: control of tachycardia and relief of anxiety.

COMPLETE INFORMATION AVAILABLE ON REQUEST.

2/2798 MK

SERPASIL® (reserpine CIBA) / ESIDRIX® (hydrochlorothiazide CIBA)
SERPASIL®-ESIDRIX® (reserpine and hydrochlorothiazide CIBA)

CIBA
SUMMIT, N. J.



Forensic Medicine

Legal Ramifications of Athletic Injuries

WILLIAM N. HARSHA

Oklahoma City

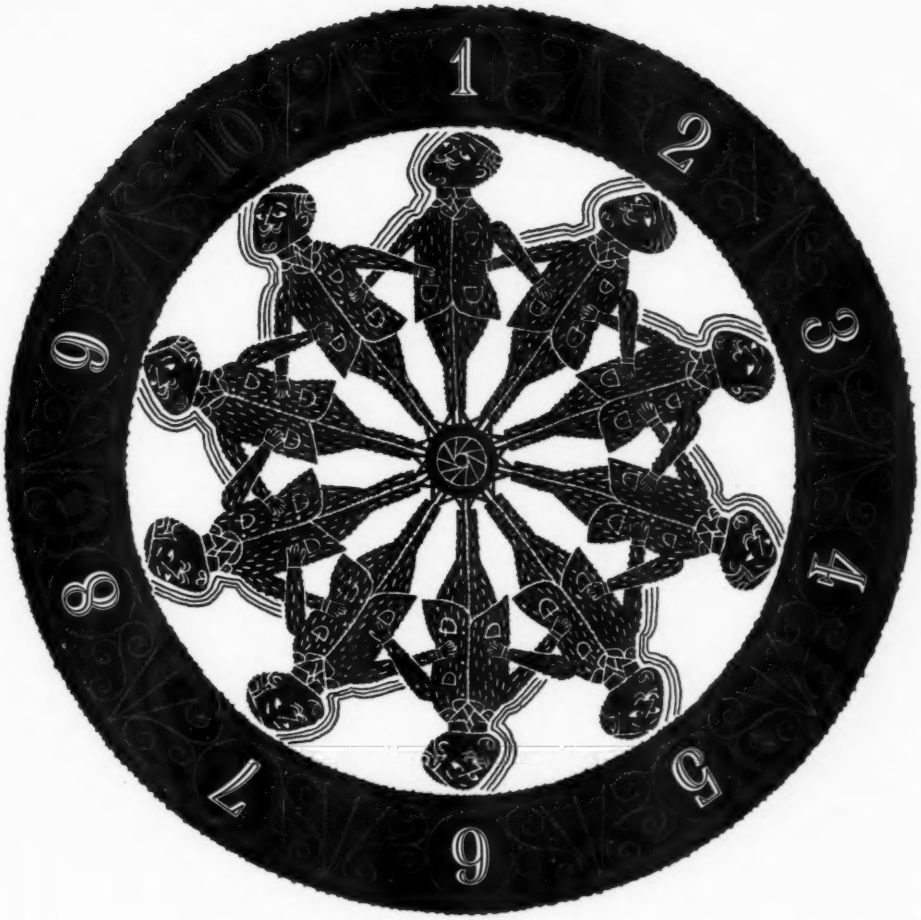
THE physician has been an integral part of athletic competition throughout history, both in the preparation of athletes for these functions and in the care of injuries. As athletics become more highly organized and as younger age groups are included, he is called on more and more to supervise and care for these youths. Paralleling the increased participation in athletic endeavors is the apparent rise in the number of litigious persons in this country, and thus it behooves all persons interested in sports to be apprised of the possible legal ramifications of athletic training and athletic injuries.

WILLIAM N. HARSHA

I have had the opportunity and the distinct honor of being the team doctor for a high school for several years and have become well acquainted with the problems of athletes as well as those of their coaches. Although lawsuits involving school districts and coaches are quite rare, all persons interested in school athletics need to be well informed concerning the possibility of such lawsuits and how to cope with the problem intelligently.

Students in high school, college, junior high school and even grammar school who engage in bona fide school athletics usually are required by the school board to sign a release for bodily injury that might result from such participation. This release, signed by parent or guardian, is a legally binding document. It protects the school board, coaches and teachers from personal liability for the usual activities of engaging in sports. The definition of "usual activities" and of what constitutes unusual activities is extremely important. Athletic endeavors that are directly controlled and supervised by the school board, coaches and teachers may be the basis for personal involvement in litigation if there is negligence on the part of these groups. Releases given by parents for the usual athletic endeavors do not include negligence or failure to recognize an injury, or direct instruction by a coach or teacher or school to play in an injured state

(Continued on page A-54)



Antivert®

STOPS VERTIGO 9 TIMES OUT OF 10!!

The latest ANTIVERT report confirms earlier findings: ANTIVERT relieves vertigo in 9 out of 10 patients. This combination of meclizine (an outstanding antihistamine for vestibular dysfunction) and nicotinic acid (the drug of choice for prompt vasodilation[1]) "... proved more effective than the use of either drug alone."[2] Out of 50 patients with Meniere's syndrome, only 4 failed to respond to ANTIVERT.[2] Prescribe one ANTIVERT tablet (12.5 mg. meclizine; 50 mg. nicotinic acid) before each meal for relief of Meniere's syndrome, arteriosclerotic vertigo, labyrinthitis and vertigo of nonspecific origin.

Supplied: **In bottles of 100 blue-and-white scored tablets. Prescription only.**

References: **1. Menger, H. C.: Clin. Med. 4:313 (Mar.) 1957. 2. Seal, J. C.: Eye Ear Nose & Throat Month. 38:738 (Sept.) 1959.**

New York 17, N. Y.
Division, Chas. Pfizer & Co., Inc.
Science for the World's Well-Being

or with inadequate equipment. For example, a high school which equips its football players with worn-out shoulder pads is not protected by the bodily-injury release, nor is the coach who instructs a player who sprains his ankle during a game to get up and run it off and returns him to the game, only to find later that a fracture with serious damage to the ankle has occurred.

A great need in our school system at present in regard to protective gear for athletes is a system of sharing the responsibility with groups competent to judge the adequacy of equipment. The average football coach is more than competent to evaluate the equipment provided for his team, but frequently the school board insists that he use worn-out, lightweight or inadequate gear. The school district, of course, incurs a very real risk if an injury of a player is due to inadequate equipment. A case in point is Govel versus Board of Education, New York, in 1944 (citation, 267 App. Div. 621). The coach, training students for a track meet, did not place mats under a set of crossbars, and one of the players fell and was injured. The mats were available, but through the coach's oversight or negligence they were not used. A judgment was returned against the board of education.

Most school districts insist on general physical examinations for athletes. Although there is no legal insistence on this practice, it offers a higher degree of protection both to the school district and to the athletes. The parent releases the child to athletic endeavors in the physical condition in which he enters the school. The school then does not have a duty to ascertain whether or not the student has a disabling medical disease. Once it does have information that he has a disabling medical disease, however, if the school or coach obliges the athlete to play, to the latter's detriment, a release by the parents of any liability for the injury becomes invalid and the school board or coaching staff assumes the risk.

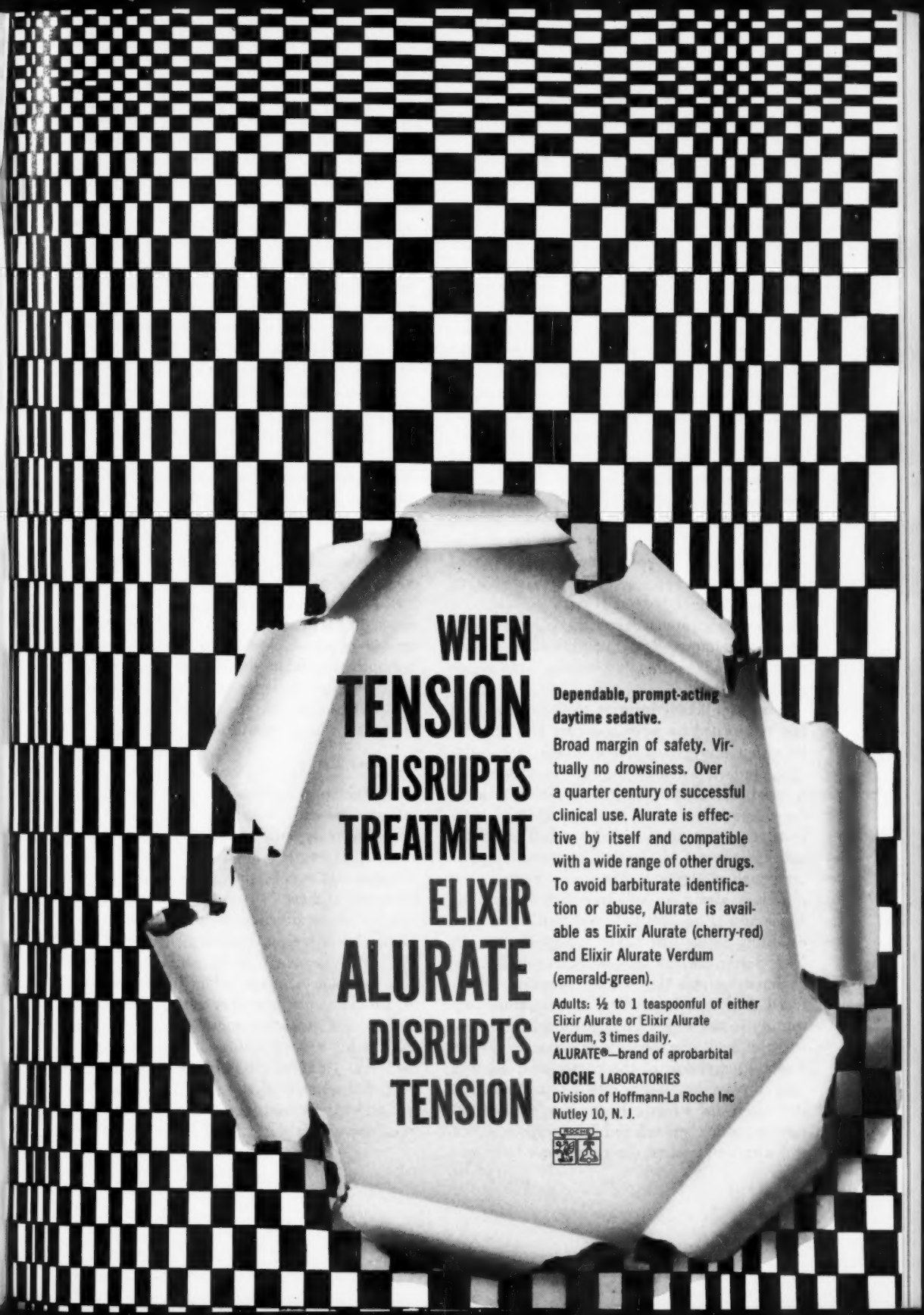
Adequate Conditioning and Training

It has been demonstrated repeatedly that the most effective way to prevent major athletic injuries is by adequate conditioning and training. High schools and colleges have active training programs for their athletes prior to competition, but in junior high and grammar schools young athletes frequently enter competitive sports with little or no conditioning. All professional people are familiar with the concept of malpractice or negligent practice, and all athletic coaches as part of their training are made keenly aware of the necessity of adequate conditioning and training. Thus the coach who assumes the responsibility of sending an unconditioned or untrained athlete into active contact competition reasonably incurs a liability for any injuries which might result. The parent who signs a release and allows his child to engage in such athletics jointly shares this liability, and it would be difficult to decide whether the coach or the parent was legally responsible if any injury based on inadequate conditioning occurred. In the case of Medsker versus Etchison in 1936 (101 Ind. App. 369) it was argued that the athletic coach was unskilled and untrained and as a result the players were not conditioned adequately and the athlete Medsker was injured. It was held that parents accept the athletic department at face value for the caliber of its coaching staff. A small school, such as the one concerned in this case, could not expect to have the expert coaching staff that a major university might have. Nonetheless this example does point up an avenue of thinking, and certainly aside from any legal ramifications it is a sound medical concept to insist on adequate training. Most high schools allow a two week training period before the first scheduled football or basketball game. This perhaps is not a long enough period, but certainly it is far better than no training period at all.

The Risk in Evaluating Athletic Injuries

The athletic coach is the key person in regard to possible negligence. Although he is automatically protected by the school board and school district, if he acts in a manner contrary to the board's instruction, he incurs total liability. In most jurisdictions the school

(Continued on page A-56)


WHEN
TENSION
DISRUPTS
TREATMENT
ELIXIR
ALURATE
DISRUPTS
TENSION
Dependable, prompt-acting daytime sedative.
Broad margin of safety. Virtually no drowsiness. Over a quarter century of successful clinical use. Alurate is effective by itself and compatible with a wide range of other drugs. To avoid barbiturate identification or abuse, Alurate is available as Elixir Alurate (cherry-red) and Elixir Alurate Verdum (emerald-green).
Adults: ½ to 1 teaspoonful of either Elixir Alurate or Elixir Alurate Verdum, 3 times daily.
ALURATE®—brand of aprobarbital
ROCHE LABORATORIES
Division of Hoffmann-La Roche Inc
Nutley 10, N. J.

board has to agree to a lawsuit before it can be sued. However, if a real cause for action is present, it is difficult for a governmental agency to refuse testing the case in court.

The evaluation of athletic injuries, particularly in football or basketball players injured during a game, constitutes a real risk to the coaching and teaching staff. Many times the coach or trainer examines such a player and, assuming the injury to be a minor sprain, returns the athlete to the game without a period of observation. In Duda versus Gains (12 N. J. Super. 326) a young athlete dislocated his right shoulder during a game. The coach examined him and told him medical treatment was unnecessary. He was returned to the game, thereby worsening his injury. A verdict against the coach was substantiated. In La-Velley versus Stanford (272, App. Div. 183) a young athlete appeared fatigued and did not perform as well as the coach felt he should. He was obliged by scholastic threats to drive himself harder, and as a result had a nervous relapse. Medical testimony was sufficient to show that the unusual energies of the coach aggravated the student's condition. A verdict was awarded against the coach. This is an extreme verdict.

Most significant injuries to the extremities are manifested by pain, swelling and deformity either immediately or within 5 to 10 minutes, and it probably is wise to remove an injured player from a game for that period of time. Another problem that arises is a player's insistence that he is not injured. The coach, perhaps against his better judgment, may return such a player to the game because the player is afraid he will lose face among his colleagues if he admits to the possibility of a disabling injury. In Sayer versus Roger (16 N. J. Super. 22) in 1951 a student deliberately acted against the coach's request and refused to submit to medical examination, continuing in the game. The decision in this case was a difficult one, because the coach did have direct supervision of the player and allowed him to play, but it was also pointed out that the coach did attempt to provide medical attention, which was refused. The verdict at first was awarded against the coach, but later was reversed; in many jurisdictions it could have been held against the coach. The coach does, of course, have absolute control of the game. It takes an astute coach to ferret out these facets of the problem.

There have been situations in which a coach has insisted that an injured player hobble off the field or in which he has examined an injured athlete in such a way as to cause further damage; the latter problem has arisen particularly in cases of injuries of the neck and low back. In one lawsuit, $200,000 was awarded to a football player whose injured neck was sharply manipulated by a member of the coaching staff on the field during examination, resulting in severe injury of the spinal cord. It is therefore imperative that the coach and the training staff be well acquainted with the types of injury that carry very real risks of permanent damage, and that they insist that players with these types of injury be carried from the field properly and that medical attention be sought promptly. Because of the possibility of such an injury in any athletic endeavor, I believe it is quite important to have a physician available at all games and promptly available during practice sessions. Most medical societies are more than ready to furnish this coverage, and it is a rare physician who is unwilling to cooperate.

Other Risks

Occasionally a coach is accused of conducting an unusually rough athletic contest or a disciplinary type of game. There have been several lawsuits in which families have charged that coaches have been unduly forceful with athletes. In certain situations this approaches negligent behavior. Pirkle versus The Oakdale Union Grammar District in 1953 (253 P2d) was a case in which the players on a football team ranged in weight from 90 to 190 lb. In a practice session one of the larger boys tackled a much smaller boy and injured his kidney and right knee. The court held that this constituted negligence on the part of the supervising coach. A further illustration of the close degree of control a coach must exercise is the case of Lee versus Board

(Continued on page A-59)

of Education (263 App. Div. 23). A baseball player in a school game was running for a high fly and stepped out into a street and was struck by a car, receiving severe injuries. It was held that the coach needed to exercise that degree of supervision to reasonably expect a fly ball to be hit into the street and to recognize the possibility that a player might be injured.

Summary

It is the duty of the school board, the athletic coach, the trainer and the teaching staff to offer athletes competent and supervised coaching and adequate protective equipment and facilities. The release which the parent or guardian signs for the participation of a child in athletics assumes that these are to be made available or, to be legally binding, must specifically exclude one of these items (and, of course, this is facetious thinking). Any member of the teaching or coaching staff can incur personal liability by acting in a fashion which a jury may consider unreasonable under the circumstances for a person trained in coaching or athletics. Avenues for incurring personal liability on the part of the person supervising the athletes are returning an injured player to the game, improper physical care of the injured player, and yielding to personal whims.

Some of the more progressive school systems recently have furnished liability insurance plans which protect school board and coaching staff. The rule in injury cases in such districts with insurance coverage has been that the insurance company can be directly held in suit without the school board's permission. This is one avenue of solving the litigation problem, but, of course, it increases the expense of athletic endeavors, which already is a problem in schools with low budgets.

An intelligent approach to the problem is to have available at all times competent medical personnel during athletic encounters, either on call for practice sessions or in the stadium or on the bench during games. All physicians should be willing to give of their time for this purpose, and most of us frankly look forward to doing it.

Books

► THE MEDICAL SOURCEBOOK

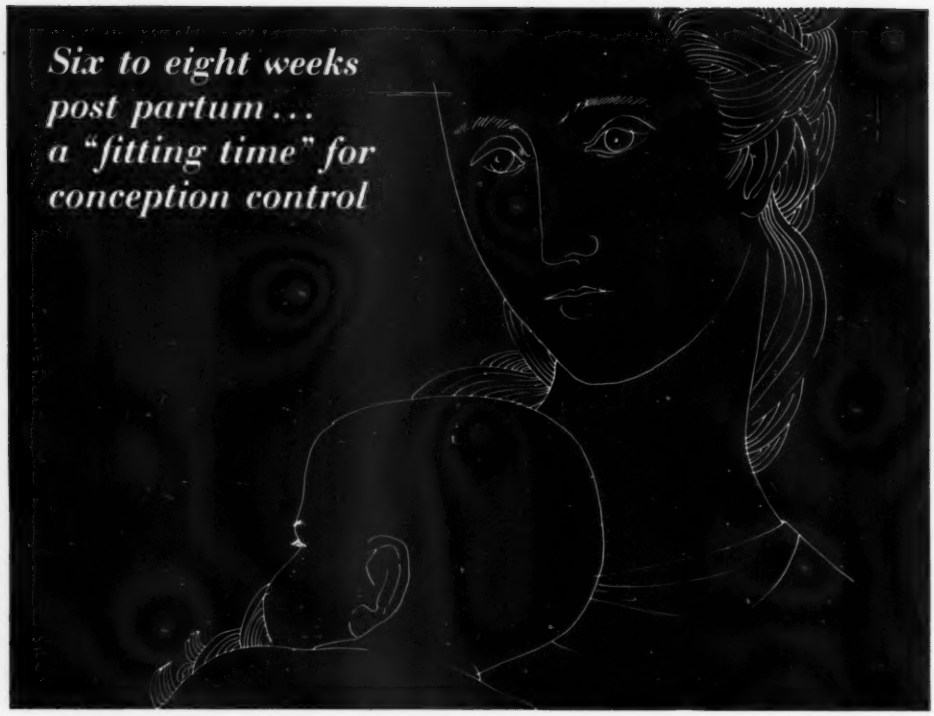
By Fred A. Mettler, M.D., Professor of Anatomy, Columbia University College of Physicians and Surgeons, New York. 1000 pages with 178 illustrations. 1959, Little, Brown & Company, Boston and Toronto. $25.00.

Dr. Mettler has designed and constructed a bridge across the chasm of misunderstanding between law and medicine. The bridge, beginning from the medical side, not only reaches the legal side but also provides good two-way intercourse. As a reference handbook for legal, legislative and administrative personnel, this work is written in simple, accurate terms. Doctors will find it a useful book to cite to lawyers, judges, hearing officers and others seeking to discuss a specific medicolegal case with a physician. The doctor can save himself time when a conference is requested by referring the legal conferee to relevant data found in this text.

Obviously, the major segment is devoted to anatomy, the traditional starting point for legal personnel with medical problems. A legal practitioner can be helped by his medical consultant if both refresh their knowledge of the specific area of the human body that is under investigation.

It would be regrettable, however, if this volume were treated by physicians and lawyers only as a reference. The introductory pages are a lucid analysis of the difficult question of how medical decisions are made in relation to legal decisions. The author's forthright concepts on persuasion, facts and values are an intelligent contribution to the philosophies of both professions in matters in which these philosophies clash when the practices overlap. Too little time is spent today in our law-medicine relationships on the basic purposes of our professions and on ways in which these

(Continued on page A-61)



Conception control becomes a matter of special concern six to eight weeks post partum, when the new mother looks to you for advice on the best way to plan the balance of her family. Reliable conception control can be virtually assured with the diaphragm and jelly method, at least 98 per cent effective.[1]

Now—cushioned comfort . . . two ways

Your patient experiences special physical comfort when you prescribe either the standard RAMSES® Diaphragm or the new RAMSES BENDEX,® an arc-ing type diaphragm.

The regular RAMSES Diaphragm, suitable for most women, is made of pure gum rubber, with a dome that is unusually light and velvet smooth. The rim, encased in soft rubber, is flexible in all planes permitting complete freedom of motion.

For those women who prefer or require an arc-ing type diaphragm, the new RAMSES BENDEX embodies all of the superior features of the conventional RAMSES Diaphragm, *together with the very best hinge mechanism contained in any arc-ing diaphragm*. It thus affords lateral flexibility to supply the proper degree of spring tension without discomfort.

RAMSES, BENDEX, and "TUK-A-WAY" are registered trademarks of Julius Schmid, Inc.

*Active agent, dodecaethyleneglycol monolaurate 5%, in a base of long-lasting barrier effectiveness.

*For added protection—RAMSES "10-Hour" Vaginal Jelly**

RAMSES Jelly is uniquely suited for use with either type of RAMSES Diaphragm. It is by design not static, but flows freely over the rim and surface of the diaphragm to add lubrication and to form a spermtight seal over the cervix, which is maintained for *ten full hours* after insertion. It is nonirritating and nontoxic.

You can now prescribe a complete unit for either type of diaphragm. RAMSES "TUK-A-WAY"® Kit #701 contains the regular RAMSES Diaphragm with introducer and a 3-ounce tube of RAMSES Jelly; RAMSES "TUK-A-WAY" Kit #703 contains the RAMSES BENDEX Diaphragm and Jelly tube. Each kit is supplied in an attractive plastic zippered case, beautifully finished inside and out. Both types are now available at key prescription pharmacies.

Reference: 1. Tietze, C.: Proceedings, Third International Conference Planned Parenthood, 1953.

Ramses® *Diaphragms and Jelly*

JULIUS SCHMID, INC. 423 West 55th Street, New York 19, N. Y.

purposes can cooperate to improve rather than confuse society through professional conflict.

Background materials on definitions, medical libraries, accident proneness, malpractice, and diagnostic technics are especially informative. A final chapter, "The most common causes of the most common complaints," offers clues to legal personnel by which to question a medical consultant. The last quarter of the book is an appendix, which includes a guide to activities, personnel, literature and societies in basic sciences and clinical medicine and a guide to standard and official terminologies. These guides are signposts to aid legal personnel in using further sources of information.

The alert medical specialist probably will also find this book valuable, not only for background matter on medicolegal problems but also in areas outside his particular specialty. Overwhelming specialization in medicine, like law, often narrows the practitioner's vision and ready knowledge. This volume will have a broadening effect.

OLIVER SCHROEDER, LL.B.

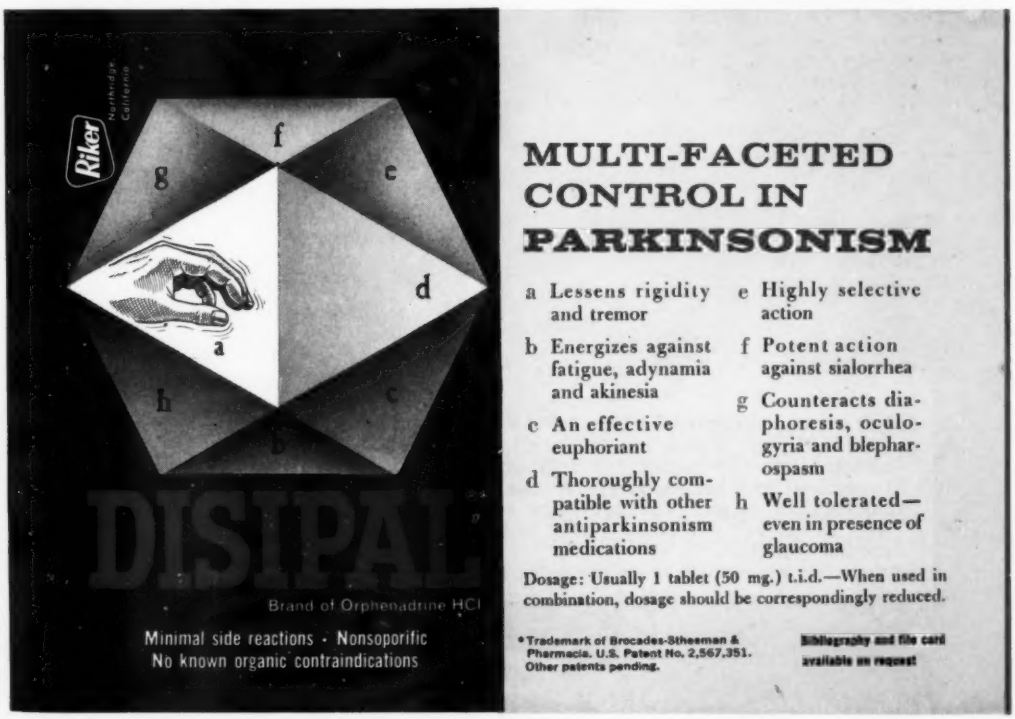
MEETINGS and Postgraduate Courses

ASSOCIATION OF AMERICAN MEDICAL COLLEGES, EVANSTON, ILLINOIS: Fellowships providing for clinical experience in foreign countries are available for medical students who have completed their third year of medical school. Applicants must be able to spend at least 12 weeks in the country of their choice. Cash awards will be made on an individual basis. Each approved medical school may nominate three applicants. Further details are available from medical school deans.

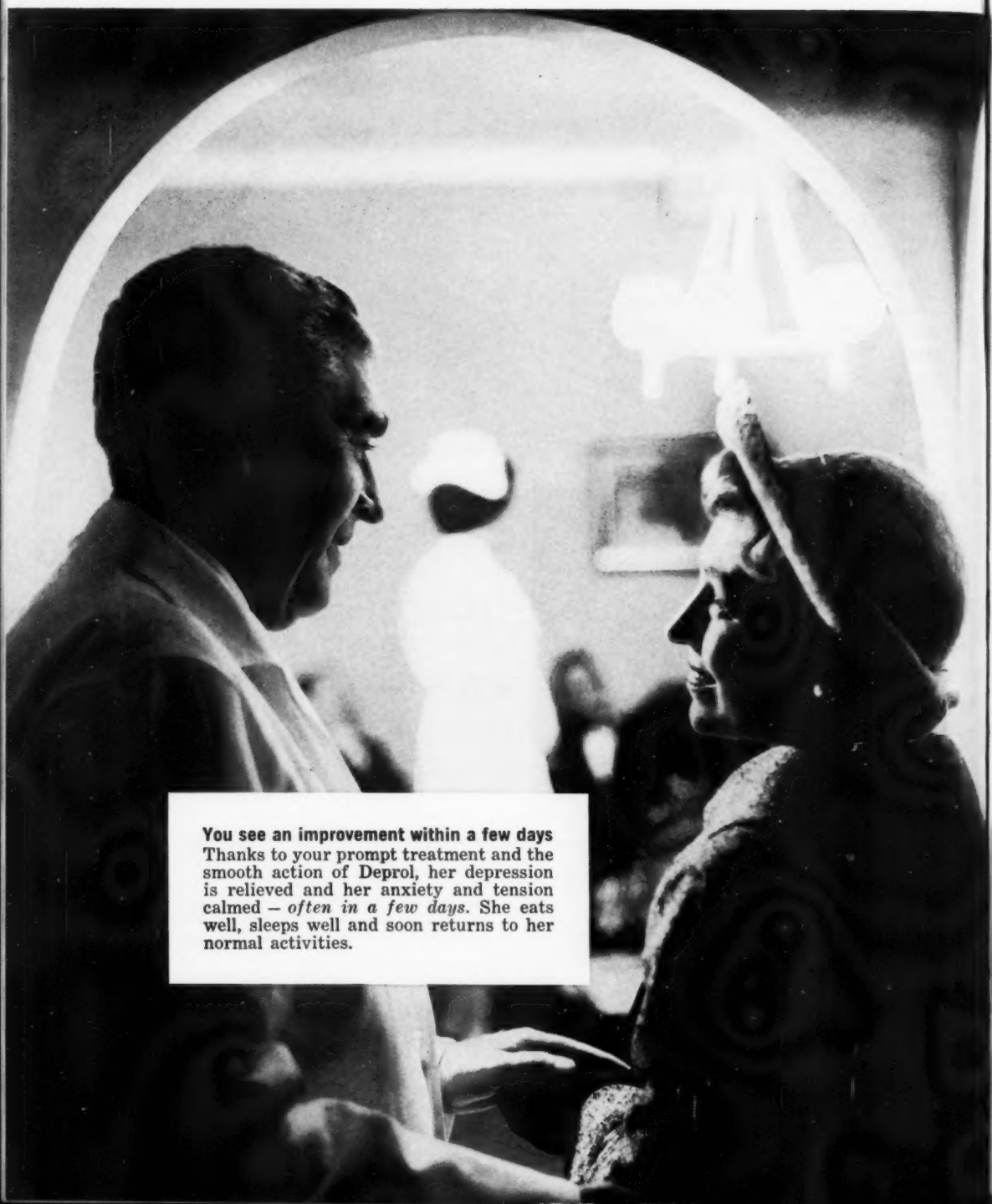
FIRST INTERNATIONAL CONGRESS OF HISTOCHEMISTRY AND CYTOCHEMISTRY, PARIS: To be held August 28-September 3. For further information, write to: Dr. R. Wegmann, Institut d'Histochimie Médicale, 45, rue des Saints-Pères, Paris (6°), France.

INTER-SOCIETY CYTOLOGY COUNCIL, CHICAGO: Annual scientific meeting to be held at the Palmer House, September 23-25. For further information, write to: Dr. Paul A. Younge, Secretary, 1101 Beacon Street, Brookline 46, Mass.

SECOND INTERNATIONAL MEETING OF FORENSIC PATHOLOGY, NEW YORK: To be held September 18-21, 1960. Meeting will include dedication of the new building for the Office of the Chief Medical Examiner, City of New York. For further information, write to: Dr. Milton Helpern, 55 East End Avenue, New York 28; Dr. Charles Larsen, Tacoma General Hospital, Tacoma 5; or Dr. Francis E. Camps, 37 Welbeck Street, London W.1, England.


Riker
Northridge, California
a
b
c
d
e
f
g
h
DISIPAL
Brand of Orphenadrine HCl
Minimal side reactions · Nonsoporific
No known organic contraindications
MULTI-FACETED CONTROL IN PARKINSONISM
a Lessens rigidity and tremor
b Energizes against fatigue, adynamia and akinesia
c An effective euphoriant
d Thoroughly compatible with other antiparkinsonism medications
e Highly selective action
f Potent action against sialorrhea
g Counteracts diaphoresis, oculogyria and blepharospasm
h Well tolerated—even in presence of glaucoma
Dosage: Usually 1 tablet (50 mg.) t.i.d.—When used in combination, dosage should be correspondingly reduced.
• Trademark of Brocades-Stheeman & Pharmacia. U.S. Patent No. 2,567,351. Other patents pending.
Bibliography and file card available on request

Lifts depression...



You see an improvement within a few days
Thanks to your prompt treatment and the smooth action of **Deprol**, her depression is relieved and her anxiety and tension calmed – *often in a few days.* She eats well, sleeps well and soon returns to her normal activities.

Radiology FOR PRACTICING PHYSICIANS

Sarcoidosis

PAUL C. HODGES*

SOME 20 years ago, in collaboration with Phemister and Brunschwig, I[1] wrote, "In the year 1899 the dermatologist Caesar Boeck reported, almost simultaneously in the Norwegian and the American literature, a disease characterized by multiple, doughy, purplish, cutaneous lesions, together with enlargement of some of the lymph nodes. Because histologically the lesions bore some resemblance to sarcoma, he suggested that the disease be called 'multiple, benign sarkoid.' Boeck recognized that sarcoid resembled a skin disease observed in 1869 by Jonathan Hutchinson in a patient named Mortimer and reported in 1899 in Hutchinson's 'Archives of Surgery' as 'Mortimer's malady,' and eventually it became clear that several others, some before, some after Boeck, had reported closely related if not identical conditions. This led to the introduction of a variety of terms, some of which are still used by dermatologists, either as descriptive of the condition as a whole or to designate subtypes. 'Sarcoid' and 'Boeck's sarcoid' are the terms in most general use today.

"Some present-day investigators are convinced that sarcoid is nothing but an unusual reaction to the ordinary tubercle bacillus working in highly resistant soil. Other workers look upon it as an infection by an organism related to but not quite identical with the tubercle bacillus. Still others feel that sarcoid and tuberculosis are distinct diseases and look upon the occasional reports of the finding of tubercle bacilli in lesions supposed to be sarcoid as errors, explained by the fact that sometimes it is difficult to differentiate between tuberculosis and sarcoid. It has been noted by many that sarcoid resembles leprosy in certain respects. All modern writers agree that sarcoid is by no means a malady confined to the skin but frequently involves as well lymph glands, spleen, lungs, bones and other tissues. Sometimes, in fact, the skin may be spared in cases where some or all of these other tissues are involved."[1]

Twenty years later the term "sarcoidosis" has come into general use; lymph gland, lung and liver biopsy and the Nickerson-Kveim test have been added as diagnostic tools; experience has been gained in recognizing the x-ray appearance of pulmonary and skeletal sarcoidosis, and serious attempts have been made to discover a possible relationship between the geographical distribution of the disease and

*Emeritus Professor and Chairman, Department of Radiology, University of Chicago, Chicago, Illinois.

some etiologic agent. At the opening of the sixth decade, however, it must be admitted that the cause of sarcoidosis is still unknown and, although steroids sometimes are helpful, no specific therapy is available. The diagnosis, clinical course and pathology of the disease are described particularly well by Longcope and Freiman,[2] Middleton,[3] Hinshaw and Garland[4] and Felson.[5] Jüngling's[6] description of the bone lesions, published in 1928 in memory of Perthes, has become a classic, and Stein, Israel and Sones[7] have brought the information up to date. In the matter of epidemiology and possible etiology Michael et al.,[8] Gentry, Nitowsky and Michael,[9] and Cummings et al.[10,11] have suggested, but by no means established, that something in denuded soils or perhaps in forests may cause sarcoidosis.

Clinical Diagnosis and Prognosis

Usually, when there are neither eye nor skin lesions sarcoidosis is clinically silent (figures 1 through 3); frequently, the pulmonary lesions disappear spontaneously (figures 1 through 4). Occasionally, the disease progresses unfavorably and eventually causes death (figure 5). Some years ago most of our cases of sarcoidosis were gleaned from patients who had long been confined to tuberculosis sanatoriums under a mistaken diagnosis of pulmonary tuberculosis, and, undoubtedly, many such patients contracted secondary tuberculosis during their sanatorium stay. Once the suspicion of sarcoidosis has been raised, a period of careful observation usually is required to establish the diagnosis; this is done partly by direct evidence and partly by exclusion. Numerous other conditions, such as berylliosis and, particularly, tuberculosis, produce pulmonary lesions strikingly like those of sarcoidosis; the glandular enlargement is similar to that in Hodgkin's disease, and the bone lesions are somewhat like those in gout.

The Nickerson-Kveim test, introduced approximately 20 years ago, is based on an antigen made from a biopsy specimen of a patient known to have sarcoidosis. The antigen is injected into the skin of a patient suspected of having sarcoidosis, and if after a period of about eight weeks a nodule forms at the site of injection this is removed and studied microscopically. The presence of typical sarcoid tissue in the excised nodule is diagnostic of sarcoidosis, and it is said that with a dependable antigen and a competent tissue pathologist to perform the test false negatives and false positives are extremely rare. Many, however, consider the test too cumbersome for practical application, and it must be admitted that it is not easy to obtain and maintain a good antigen. Of at least as much importance and much more widely employed is the microscopic examination of a scalene lymph gland obtained at biopsy or of biopsy material from lung or spleen.

Tuberculosis must be excluded by repeated negative sputum and gastric washings and negative guinea pig inoculations of biopsy material. If in addition to all this the tuberculin skin test is negative, the presumptive evidence for a diagnosis of sarcoidosis becomes even stronger.

Histology

The microscopic appearance of sarcoid tissue was described as follows in 1948 at a conference sponsored by the National Research Council: "Pathologically [sarcoidosis] is characterized by the presence in any organ or tissue of epithelioid-cell tubercles with inconspicuous or absent necrosis and by the frequent presence of refractal or apparently calcified bodies in the giant cells of the tubercles. The characteristic lesion may be replaced by fibrosis, hyalinization or both."

Whether the tissue be lymph gland, lung parenchyma, heart muscle, spleen, or bone, in sarcoidosis it is tissue such as this which "repeats itself with monotonous regularity."

X-ray Diagnosis

Pulmonary lesions—All observers agree that the pulmonary lesions fall into three main groups, and some contend that there is a more or less regular progression from one phase to another. These phases are (1) glandular enlargement alone, (2) glandular enlargement plus parenchymal involvement, and (3) parenchymal involvement alone.

Glandular enlargement usually is bilateral

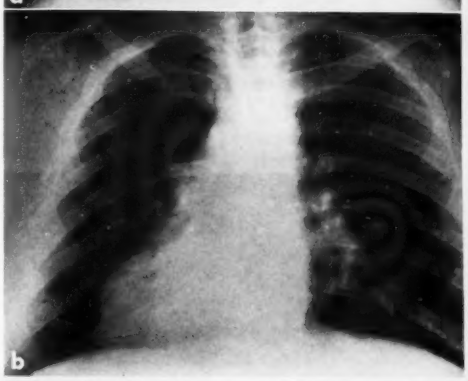
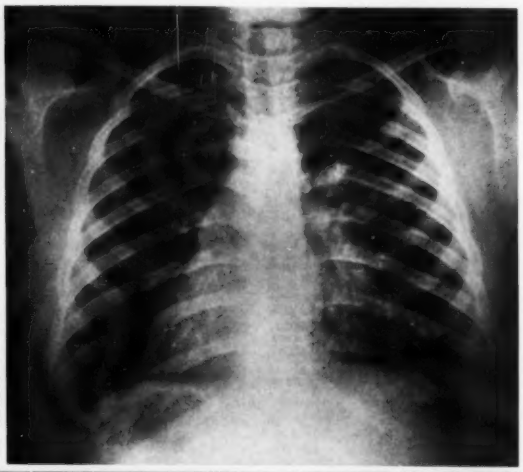


FIGURE 1. a. Glandular sarcoidosis in a 15 year old boy, with enlarged tracheobronchial glands on both sides and enlarged paratracheal glands on the right side.

b. The masses began to recede within six months; 14 months later, they had disappeared without treatment.

FIGURE 2. Symptomless unilateral pulmonary sarcoidosis in a 12 year old girl. The lesions, which were much more obvious on the right side, were picked up at routine chest microfilming. No skeletal lesions were found.



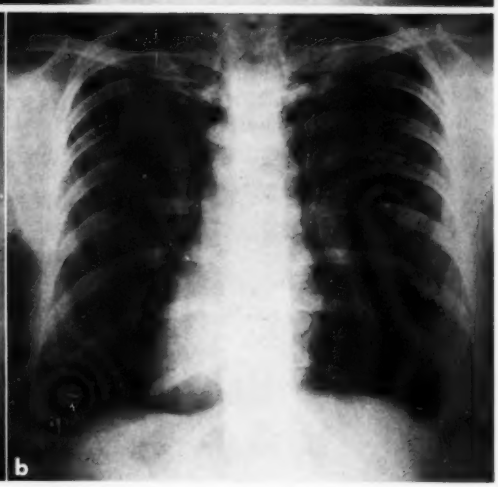


FIGURE 3. a. Symptomless bilateral pulmonary lesions of sarcoidosis found at routine microfilming in a 30 year old woman student.

b. Spontaneous remission occurred and the lungs were clear two years later.

A lesion in one of the fingers (see figure 8), the absence of clinical evidence of tuberculosis, and the spontaneous remission argued strongly for the diagnosis of sarcoidosis in spite of the fact that no biopsy was done and results of the Nickerson-Kveim test were negative.

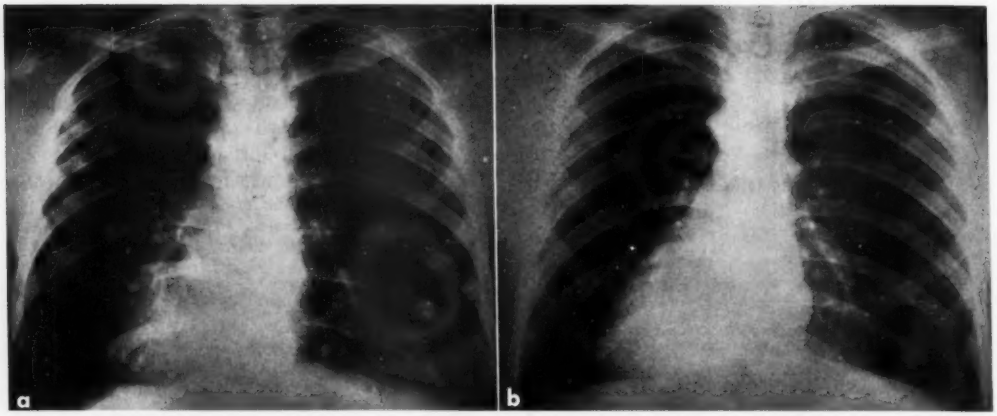


FIGURE 4. a. Pulmonary sarcoidosis simulating metastatic neoplasm, seen on admission of patient.

b. Three years later, total clearing had occurred without treatment.

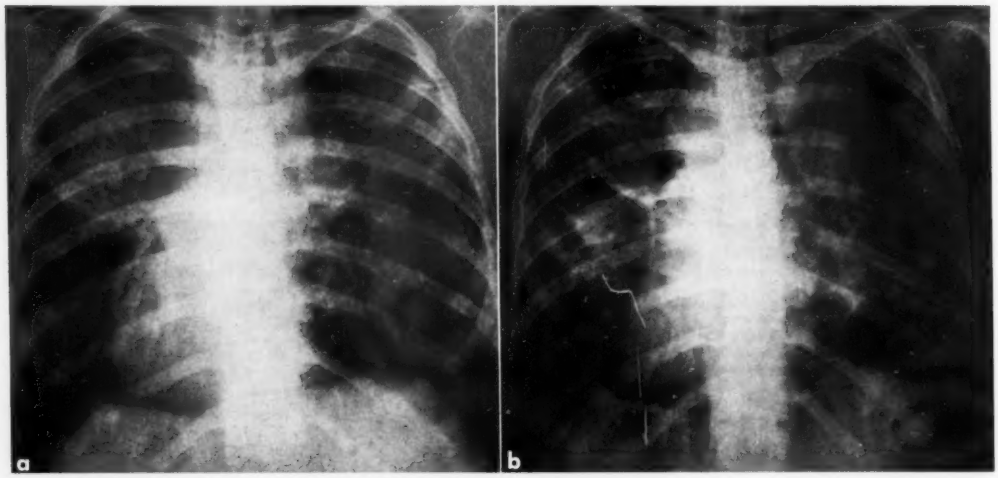


FIGURE 5. a. Severe generalized sarcoidosis, diagnosed in a patient who had spent several years in a sanatorium because of supposed tuberculosis in spite of the absence of tubercle bacilli.

b. Appearance of lesions eight and one-half years later, shortly before the patient died.

Skeletal lesions were present in fingers and toes (see figure 7). Five years before death, pus drained from an axillary abscess was positive for tubercle bacilli, but at autopsy lesions in lungs, lymph nodes, spleen and adrenals were found to be sarcoid.

although seldom symmetric. Both hilar and paratracheal glands may be involved, or one set alone may be affected. Sarcoid nodulation in the lung parenchyma may be so small and so uniformly distributed as to look almost like pneumonia. More commonly, the nodules are clumped into approximately spherical lesions 2 cm. or more in diameter with borders which Felson described as "fluffy"; they may reach a diameter of 5 cm. or more and be mistaken for cannon-ball metastases (figure 6).

Undoubtedly, many of the cases of sarcoid-

FIGURE 6. Unusual type of nodular pulmonary sarcoidosis in a 19 year old girl. Results of a scalene node biopsy were positive. No skeletal lesions were found.

FIGURE 7. *Left.* In the patient described in figure 5, typical lesions of skeletal sarcoidosis were observed in the proximal phalanx of the first digit on the right hand. Similar lesions were seen elsewhere in the feet and in the hands.

FIGURE 8. *Right.* Lesion of skeletal sarcoidosis in the middle phalanx of the fourth digit of the right hand of the patient described in figure 3.

osis reported in former years were complicated by fibrocaseous tuberculosis, but it has been established that in severe progressive sarcoidosis that disease alone can reproduce almost all the x-ray findings which we have hitherto considered to be typical of tuberculosis (figure 5).

Skeletal lesions—In perhaps 17 per cent of all cases of sarcoidosis, a careful x-ray examination of the fingers and toes will reveal skeletal lesions, and the incidence is much higher when there is cutaneous sarcoidosis of the fingers and toes. The most characteristic lesion (figure 7) is a localized coarsening of the

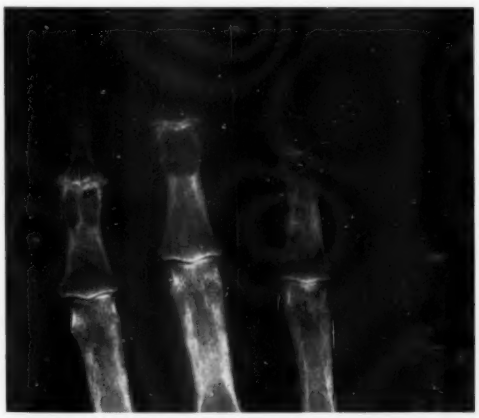


FIGURE 9. Lesions of skeletal sarcoidosis in several bones of the right hand of a 51 year old woman who had no pulmonary lesions.

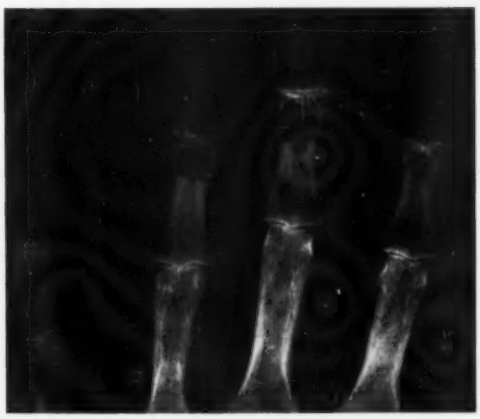


FIGURE 10. In the left hand of the patient in figure 9, a sarcoid nodule caused a pathologic fracture of the middle phalanx of the fifth digit.

trabecular pattern of one of the phalanges. Instead of the regular, fine-grain meshwork of the normal cancellous bone, one sees a series of small, irregular vacuoles replacing the normal pattern. In microcosm the appearance is something like that of an ear of sweet corn in which a segment of the regular rows of uniform-sized grains is replaced by malformed, irregular, larger grains.

More common but not quite so characteristic are the so-called punched-out lesions of sarcoidosis (figures 8 and 9). Occasionally, these lead to pathologic fracture (figure 10), and, when they are located in the terminal phalanx and are accompanied by cutaneous lesions, partial spontaneous amputation may take place.

Usually, skeletal lesions are symptomless and are important principally as another link in the chain of diagnostic evidence.

REFERENCES

1. Hodges, P. C., Phemister, D. B. and Brunschwig, A.: The Roentgen Ray Diagnosis of Diseases of the Bones and Joints. New York, Thomas Nelson & Sons, 1938, p. 214.
2. Longcope, W. T. and Freiman, D. G.: A study of sarcoidosis. Medicine 31:1-132, 1952.
3. Middleton, W. S.: The riddle of sarcoidosis. Ann. Int. Med. 41:465-478, 1954.
4. Hinshaw, H. C. and Garland, L. H.: Diseases of the Chest. Philadelphia, W. B. Saunders, 1956, pp. 561-577.
5. Felson, B.: Less familiar roentgen patterns of pulmonary granulomas. Am. J. Roentgenol. 81:211-223 (February) 1959.
6. Jüngling, O.: Über ostitis tuberculosa multiplex cystoides. Beitr. klin. Chir. 143:401-475, 1928.
7. Stein, G. N., Israel, H. L. and Sones, M.: A roentgenographic study of skeletal lesions in sarcoidosis. A.M.A. Arch. Int. Med. 97:532-536, 1956.
8. Michael, M., Jr., Cole, R. M., Beeson, P. B. and Olson, B. J.: Sarcoidosis—preliminary report on a study of 350 cases with special reference to epidemiology. Am. Rev. Tuberc. 62:403, 1950.
9. Gentry, J. T., Nitowsky, H. M. and Michael, M.: Studies on the epidemiology of sarcoidosis in the United States—the relationship to soil areas and to urban-rural residents. J. Chem. Invest. 34:1839-1856, 1955.
10. Cummings, M. M., Dunner, E., Schmidt, R. H., Jr. and Barnwell, J. B.: Concepts of epidemiology of sarcoidosis. Preliminary report of 1,194 cases reviewed with special references to geographic ecology. Postgrad. Med. 19:437-446, 1956.
11. Cummings, M. and Hudgins, P. C.: Chemical constituents of pine pollen and their possible relationships to sarcoidosis. Am. J. M. Sc., n.s., 236:311-317, 1958.

Detailed Information on

TABLETS

Equagesic

Meprobamate and Ethoheptazine Citrate with Acetylsalicylic Acid

A Century of Service to Medicine

Composition

Each EQUAGESIC tablet contains 150 mg. meprobamate, 75 mg. ethoheptazine citrate (1-methyl-4-carbethoxy-4-phenyl hexamethylenimine citrate) and 250 mg. acetylsalicylic acid.

Action

Ethoheptazine (Zactane®) was first synthesized in the Wyeth Institute for Medical Research. The general pharmacological properties and analgesic potency of ethoheptazine in animals have been reported. The clinical effectiveness and safety of this compound have been reported by Grossman, Golbey, Cass, and Batterman and their colleagues. In summary, ethoheptazine is an active analgesic which does not cause sedation, disorientation, constipation, suppression of cough reflex or change in pupil size, nor does it have addiction liability. The combination of ethoheptazine and acetylsalicylic acid (Zactirin®) in the recommended dosage has been found to be equivalent to codeine and acetylsalicylic acid in analgesic potency. The effectiveness and safety of Zactirin for relief of the common types of pain have been reported by several investigators.

The pharmacological action of meprobamate has been carefully studied and described in detail by Berger. This compound, although resembling mephenesin in structure, differs pharmacologically in that its anticonvulsant properties are more profound, its muscle-relaxant effect is of longer duration, it possesses an unusual type of sedative effect not common to either mephenesin or the barbiturates, and, finally, it is active when administered by the oral route. Meprobamate has been proved clinically effective as a skeletal muscle relaxant in patients with neurological conditions, rheumatic disorders, trauma, and as an adjunct to physiatric management of musculoskeletal and neuromuscular disorders. Meprobamate has been shown to be of considerable value in the management of anxiety and tension occurring alone or as an accompanying symptom complex to medical and surgical disorders and procedures.

A combination of meprobamate and acetylsalicylic acid was found by Mitchell to be a useful and safe medication for the treatment of skeletal muscle spasm of varied causes, such as myalgias due to infectious diseases; states of anxiety, tension, and nervousness; premenstrual tension and primary dysmenorrhea; and functional headache. Splitter used EQUAGESIC in patients suffering from musculoskeletal pain associated with muscle spasm and anxiety or tension and found it to be an effective therapeutic agent.

The practicing physician's use of Zactirin administered simultaneously with meprobamate for the relief of muscle spasm and anxiety associated with common painful conditions caused us to prepare the combination oral dosage form. Investigators using meprobamate and ethoheptazine with acetylsalicylic acid tablets have reported this combination to be an effective anti-anxiety, muscle-relaxant analgesic with low side effect liability.

Indications

EQUAGESIC is an effective and well tolerated anti-anxiety, skeletal-muscle-relaxant analgesic and may be used for relief of pain which is accompanied by either skeletal muscle spasm or tension and anxiety or both.

Administration and Dosage

The usual dosage of EQUAGESIC is one or two tablets three or four times daily as needed for the relief of pain and accompanying skeletal muscle spasm or anxiety.

Side Effects

Serious side effects have not been observed following the administration of EQUAGESIC. A small percentage of patients may experience nausea with or without vomiting and epigastric distress. Dizziness occurs but rarely when EQUAGESIC is administered in the recommended dosage. The meprobamate may cause drowsiness but, as a rule, this disappears as the therapy is continued. Should drowsiness persist, this symptom can usually be controlled by decreasing the dose. It may be desirable in some instances to administer central stimulants such as amphetamine or mephentermine sulfate concomitantly to control drowsiness.

On rare occasions, meprobamate has caused severe allergic reactions. This has occurred in most instances in patients who have had only 1-4 doses of meprobamate and have not had a previous contact with the drug. Previous history of allergy does not appear to be related to the incidence of reactions. Mild reactions are characterized by an itchy urticarial or erythematous, maculopapular rash which may be generalized or confined to the groins. Acute non-thrombocytopenic purpura with cutaneous petechiae, ecchymoses, peripheral edema and fever have also been reported. More severe cases, observed only very rarely, may also have fever, fainting spells, angioneurotic edema and bronchial spasm. Treatment consists of the administration of epinephrine, an antihistaminic and, possibly, hydrocortisone or similar agents. Meprobamate should be stopped and reinstitution of therapy should not be attempted.

EQUAGESIC or any of the ingredients used separately in the recommended dosage (Zactane®, Zactirin®, Equanil®) has not been reported to have caused constipation, change in pupil size, disorientation, any significant degree of tolerance, or untoward effects on the formed elements of the blood or cardiovascular system.

Caution

Preparations containing acetylsalicylic acid should be kept out of the reach of children.

Careful supervision of dose and amounts prescribed for patients is advised, especially with those patients with a known propensity for taking excessive quantities of drugs. Excessive and prolonged use of meprobamate in susceptible persons, for example, alcoholics, former addicts, and other severe psychoneurotics, has been reported to result in dependence on the drug. Where excessive dosage has continued for weeks or months, dosage should be reduced gradually rather than abruptly stopped since withdrawal of a "crutch" may precipitate withdrawal reactions of greater proportions than the original indication for prescription. Abrupt discontinuance of doses in excess of the recommended dose has resulted in some cases in the occurrence of epileptiform seizures.

EQUAGESIC should not be given to individuals with a history of sensitivity or severe intolerance to acetylsalicylic acid or meprobamate.

Instances of accidental or intentional significant overdosage with ethoheptazine combined with acetylsalicylic acid (Zactirin) have been reported to produce mild depression, drowsiness, and a feeling of light-headedness, with uneventful recovery. Appropriate therapy of the signs and symptoms as they appear is the only recommendation possible at this time. Overdosage with ethoheptazine combined with acetylsalicylic acid (Zactirin) would probably produce the usual symptoms and signs of salicylate intoxication. Observation and treatment should include induced vomiting or gastric lavage, specific parenteral electrolyte therapy for keto-acidosis and dehydration, watching for evidence of hemorrhagic manifestations due to hypoprothrombinemia which, if it occurs, usually requires whole blood transfusions.

Suicidal attempts with meprobamate have resulted in coma, shock, vasomotor and respiratory collapse. Although up to this time very few of these have been successful in spite of ingestion of large amounts of the drug, doses greater than those recommended may be hazardous. Meprobamate should be given cautiously, and in small amounts, to patients who have suicidal tendencies. In cases where excessive doses have been taken, therapy is symptomatic and may include central stimulants, pressor amines and careful observation. Sleep ensues rapidly after excessive dosage but is normal in character, with blood pressure, pulse and respiratory rates reduced to basal levels.

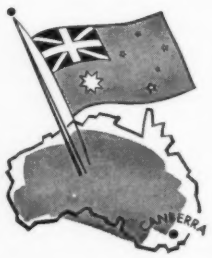
References available on request

Wyeth Laboratories Philadelphia 1, Pa.

Medicine from Abroad

FROM POSTGRADUATE MEDICINE'S CORRESPONDENTS

AUSTRALIA



Staphylococcal pneumonia in infants —Dr. Robert Morris, Mater Hospital, Newcastle, New South Wales, has reported that infantile staphylococcal pneumonia, once rarely seen, is now one of the most common serious diseases observed in pediatric practice. He discussed 18 cases encountered in a children's ward at a country center over a period of 20 months, which emphasized the dangers incumbent on increasing dissemination of staphylococci in the Australian population.

All patients in this series were two years old or less when they were admitted to the hospital; the youngest was 16 days of age. Thirteen patients were six months old or less. Diagnoses on admission were pneumonia or bronchopneumonia in 14 cases, pleural effusion in two cases, and tracheobronchitis and pyrexia of unknown origin in the two remaining cases. The diagnoses were based on clinical, radiologic and, when possible, bacteriologic findings.

The 18 patients were under the care of several practitioners, and there was no set routine of treatment. Various antibiotics and combinations of antibiotics were used to counteract the infection. In seven cases, empyema was treated by pleural catheterization and underwater drainage. In four of these latter cases, bronchopleural fistulas developed but did not warrant any specific treatment. In one case, the thick fibrinous nature of the pus necessitated thoracotomy as well as decortication.

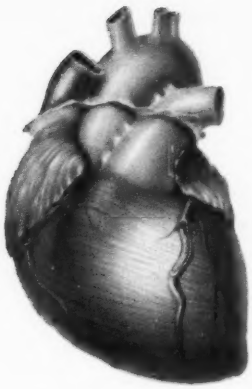
The increasing frequency of staphylococcal infection of the lungs and pleura in infants has been noted in Great Britain, Canada and America as well as in Australia.

Dr. Clair Isbister, Royal North Shore Hospital, Sydney, stated that in September 1958, the New South Wales Department of Public Health added the following staphylococcal infections to its list of notifiable infectious diseases: mastitis, pneumonia and infections occurring in infants less than four weeks old. This procedure was recommended by the New South Wales branch of the British Medical Association as a result of the serious outbreak of staphylococcal infections in the past year and the possibility of another such epidemic in the near future.

A serious staphylococcal infection rarely occurs in the first month of life without having been preceded by a minor infection or by some condition which temporarily lowers the baby's resistance to infection. Dr. Isbister stated that circumcision may be such a factor.

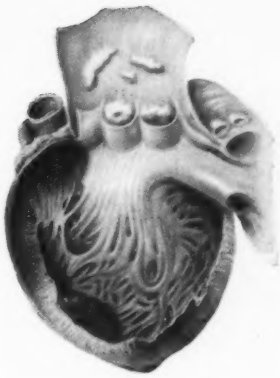
The clinical manifestations of infection in the first two weeks of life may be very unimpressive due to the baby's apparent inability to localize infection; therefore, quite trivial lesions must be treated with respect. The common infections which can occur during the first two weeks of life are conjunctivitis, pustular rashes, paronychia, nasopharyngitis with purulent discharge, redness of or discharge from the umbilicus, otitis

(Continued on page A-88)



IN ANGINA PECTORIS AND CORONARY INSUFFICIENCY

... the treatment must go further than vasodilation alone. It should also control the patient's ever-present anxiety about his condition, since anxiety itself may bring on further attacks.



AFTER MYOCARDIAL INFARCTION

... it is frequently not enough to boost blood flow through arterial offshoots and establish new circulation. The disabling fear and anxiety that invariably accompany the condition must be reduced, or the patient may become a chronic invalid.

Protects your coronary patient better than vasodilation alone

Unless the coronary patient's ever-present anxiety about his condition can be controlled, it can easily induce an anginal attack or, in cases of myocardial infarction, considerably delay recovery.

This is why Miltrate gives better protection for the heart than vasodilation alone in coronary insufficiency, angina pectoris and postmyocardial infarction. Miltrate contains not only PETN (pentaerythritol tetranitrate), acknowledged as basic therapy for long-acting vasodilation. What is more important – Miltrate provides Miltown, a tranquilizer of *proven* effectiveness in relieving anxieties, fear and day-to-day tension in over 600 clinical studies.

Thus, your patient's cardiac reserve is protected against his fear and concern about his condition...and his operative arteries are dilated to enhance myocardial blood supply.

Supplied: Bottles of 50 tablets. Each tablet contains 200 mg. Miltown and 10 mg. pentaerythritol tetranitrate.
Dosage: 1 or 2 tablets q.i.d. *before meals* and at bedtime, according to individual requirements.

REFERENCES

1. Ellis, L. B. *et al.*: Circulation *17*:945, May 1958. **2.** Friedlander, H. S.: Am. J. Cardiol. *1*:395, Mar. 1958. **3.** Riseman, J. E. F.: New England J. Med. *261*:1017, Nov. 12, 1959. **4.** Russek, H. I. *et al.*: Circulation *12*:169, Aug. 1955. **5.** Russek, H. I.: Am. J. Cardiol. *3*:547, April 1959. **6.** Tortora, A. R.: Delaware M. J. *30*:298, Oct. 1958. **7.** Waldman, S. and Pelner, L.: Am. Pract. & Digest Treat. *8*:1075, July 1957.

Miltrate®

Miltown® (meprobamate) + PETN

WALLACE LABORATORIES / *New Brunswick, N.J.*

CML-1388

media, infected skin abrasions, and indurated areas of the skin. The more serious infections, which tend to occur a little later (from the second to the seventh week), are abscesses, cellulitis, osteomyelitis, osteitis and septic arthritis, pneumonia and pyelonephritis (the last-mentioned is insidious and, like otitis media, very easy to miss).

Treatment is still that recommended in the National Health and Medical Research Council's "blue booklet," but hexachlorophene is now being widely used as pHisoHex® baths, and hibitane® ointment seems as effective as the local application of antibiotics and is probably a wiser choice of treatment. Any baby showing general symptoms, such as refusal of food, lethargy, pyrexia, jaundice or rapid respiration, in association with a local lesion will usually require antibiotics administered orally or parenterally; septicemia and multiple blood-borne abscesses are always a possibility.

AUSTRIA

Excision of cerebral hemispheres—Problems involved in excising the cerebral hemispheres were discussed at a meeting of the Society of Physicians in Vienna. Dr. Kundratitz pointed out that for children who have a brain injury with severe pathologic and anatomic changes, only neurosurgical intervention can effect considerable improvement or cure. Results of pneumoencephalography, electroencephalography and angiography, together with the clinical findings, establish the exact diagnosis and indications for operation.

The principal indications for operation are severe cerebral changes in cases of spastic infantile hemiplegia associated with epileptic fits which cannot be controlled by medicaments. However, Dr. Kundratitz stated that hemispherectomy should be performed in certain cases even if there have been no attacks of cerebral convulsions, because the diseased and pathologically changed portion of the brain represents grave danger and possible injury to the other cerebral hemisphere. This operation is usually performed only if the second hemisphere is still normal or just slightly changed; however, an exception should be made in some cases, since a cerebral hemisphere which is only slightly altered or is being altered gradually can return to normal after the source of injury has been eliminated.

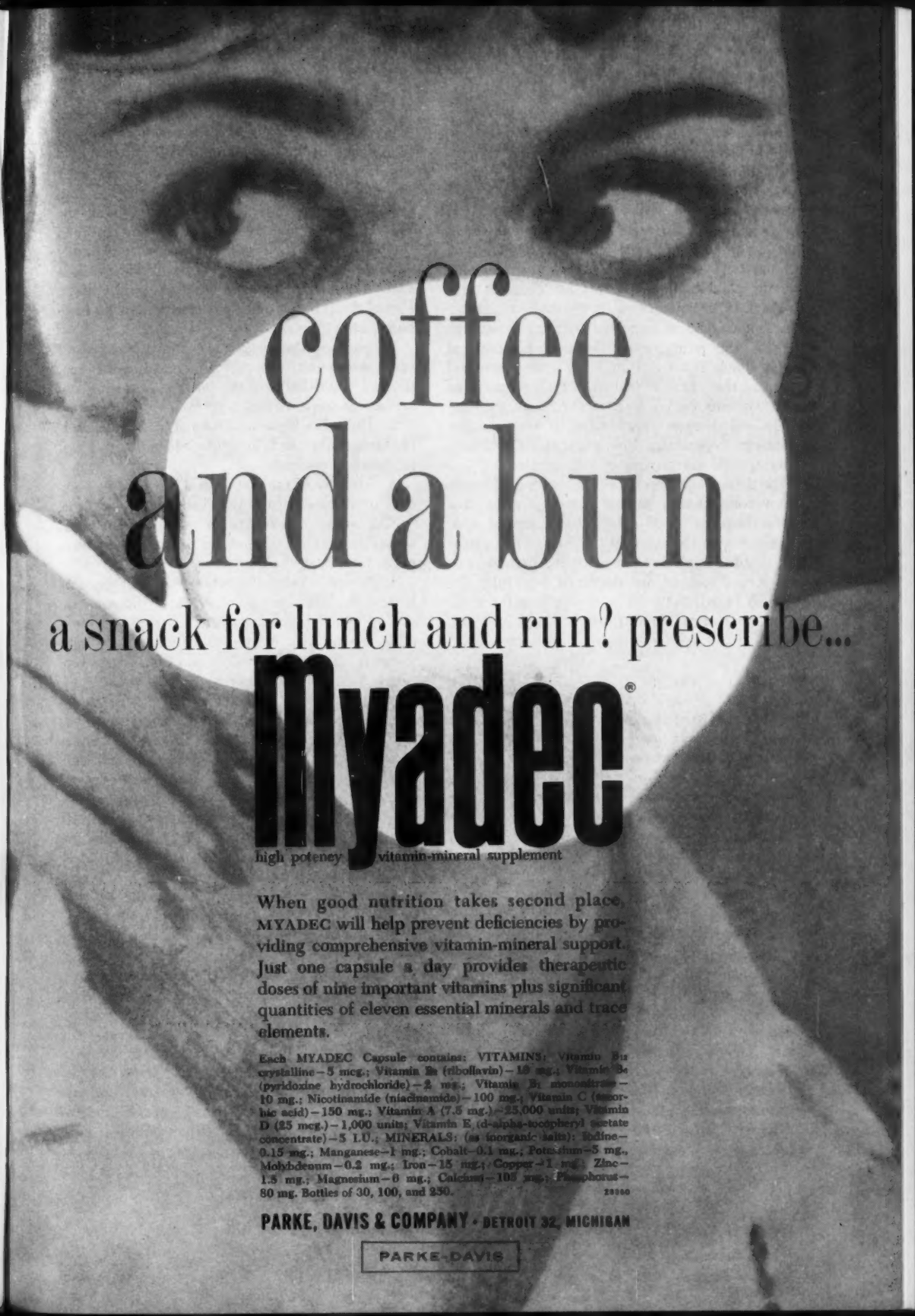
The lecturer illustrated his statements by presenting the case of a five year old boy who had a large porencephalic cyst of the temporal and parietal lobes and sclerosing atrophy of the brain. The condition had progressed so far that the second hemisphere was pulled to the other side, the ventricles were moderately widened, and the electroencephalogram showed pathologic configurations. Three months after hemispherectomy, improvement was evidenced by convulsions of the left upper and lower extremities, which permitted voluntary movement of the arm and walking with support. The electroencephalogram was normal.

Results achieved in this case should stimulate other physicians to perform this operation in selected patients and to consider additional indications for operation. Certain lesions of the second hemisphere should not contraindicate operation, because with surgery this hemisphere can be protected from further damage and even be returned to normal.

Dr. Kraus stated that excision of the cerebral hemisphere is based on the work of Krynauw, who suggested this procedure as a way of freeing patients from epileptic attacks and mental changes. In this operation, a large osteoplastic trephining is performed; after the dura is opened, the middle cerebral artery is closed by clamps distally from the branching site of the anterior choroid artery and is cut, if it has not already obliterated itself. Then the veins which run from the edge of the mantle to the sagittal sinus are coagulated and cut. The lateral ventricle is opened widely from the direction of the corpus callosum, and the entire hemisphere, with the exception of the basal ganglions, is removed.

Dr. Huber described a case of Little's disease in which a hemispherectomy of the left side was performed. Four years after the operation, the child could walk and talk; however, the epileptic attacks were stopped for only a year and a half. The preoperative and postoperative electroencephalographic findings in this case were given by Dr. Pateisky. The abnormal electroencephalographic signs found on the organically less damaged side preoperatively were considered as indicative of a spreading functional disturbance of the organically more seriously damaged hemisphere, not as a contraindication for performing hemispherectomy.

(Continued on page A-90)


coffee
and a bun
a snack for lunch and run? prescribe...
Myadec®
high potency vitamin-mineral supplement
When good nutrition takes second place, MYADEC will help prevent deficiencies by providing comprehensive vitamin-mineral support. Just one capsule a day provides therapeutic doses of nine important vitamins plus significant quantities of eleven essential minerals and trace elements.
Each MYADEC Capsule contains: VITAMINS: Vitamin B12 crystalline—5 mcg.; Vitamin B2 (riboflavin)—10 mg.; Vitamin B6 (pyridoxine hydrochloride)—2 mg.; Vitamin B1 mononitrate—10 mg.; Nicotinamide (niacinamide)—100 mg.; Vitamin C (ascorbic acid)—150 mg.; Vitamin A (7.5 mg.)—25,000 units; Vitamin D (25 mcg.)—1,000 units; Vitamin E (d-alpha-tocopheryl acetate concentrate)—5 I.U.; MINERALS: (as inorganic salts): Iodine—0.15 mg.; Manganese—1 mg.; Cobalt—0.1 mg.; Potassium—5 mg., Molybdenum—0.2 mg.; Iron—15 mg.; Copper—1 mg.; Zinc—1.5 mg.; Magnesium—6 mg.; Calcium—105 mg.; Phosphorus—80 mg. Bottles of 30, 100, and 250. 23350
PARKE, DAVIS & COMPANY · DETROIT 32, MICHIGAN
PARKE-DAVIS

Dr. Tschabitscher mentioned that following hemispherectomy improvement is noted first in focal epilepsy, then in the psychomotor mechanism, and finally in the disturbed motility of the paretic side. This is explained by the fact that excision of the diseased hemisphere reactivates the homolateral fibers of the corticospinal tract and enables normal impulses to be delivered to the paretic extremities. The importance of sparing the caudate nucleus and the thalamus was stressed. If the caudate nucleus is removed, motor function cannot be expected to return, perhaps because the pathway of the new homolateral motor function runs through the extrapyramidal fibers of the caudate nucleus. Although most of the symptoms (sensibility, motor function, athetosis) will disappear or return to normal after operation, contralateral hemianopsia will always remain, with the sparing of the macula.

The theory and practical performance of hemispherectomy should be considered in terms of a dysfunction, as opposed to the old idea of nonfunctioning of the cerebral capacity. This operation should be carried out while the patient is in early childhood, before the brain has fully developed. This is the most favorable time for restitution, regeneration and transmission of function.

BRAZIL

South American blastomycosis and Hodgkin's disease—The coexistence of deep mycosis with malignant disease of the reticuloendothelial system seems to be more than coincidence, as evidenced by the numerous reports appearing in the medical literature. In *O Hospital*, D. L. Altério and G. Del Negro briefly reviewed the literature and discussed a patient with South American blastomycosis in whom a clinical and histologic picture of Hodgkin's disease developed many years later. Apparently, the blastomycosis was not active when the malignant lymphogranulomatosis developed. The authors called attention to the fact that the coexistence of Hodgkin's disease accounts for the failure of specific treatment for the mycosis.

Biopsy of the duodenum and jejunum—In *Revista da Associação medica brasileira*, H. Espejo, T. Morais, J. de S. Meireles, M. R. Montenegro and J. F. Pontes presented the results of 69 biopsies of the duodenum and jejunum. Good results were obtained in 41 cases; in 28 cases (41 per cent), the results were classified as failures. Gastric biopsy was performed with the Shiner, Crosby and Australian tubes as modified by the authors. The best specimens were obtained with the Crosby tube, since this device is more easily handled and causes very little discomfort. Use of the tube is indicated in patients who have had gastrectomy.

Because of the relatively small number of cases, no definite conclusions regarding histopathology could be reached, but the following observations were made:

1. There is a high incidence of atrophic glands of Lieberkühn and atrophic villosities in gastrectomized patients.
2. Atrophy of the glands and the villosities occurs in all cases of the malabsorption syndrome.
3. Eosinophil infiltrate in patients with parasitosis is similar to that in patients who have undergone partial gastrectomy.
4. Atrophic villosities were found in patients with striking histologic changes of the mucosa.
5. Slight inflammatory cell infiltrate and moderate irregularity in the villosities, which were found in nearly all cases, do not necessarily represent a pathologic finding.

Asthma—After considering the concept, pathogenesis and symptomatology of asthma and the controversies concerning these factors, W. Lages emphasized the importance of psychogenic factors in the genesis of the syndrome. He urged pediatricians to be more cognizant of such elements, from both a diagnostic and a therapeutic standpoint, and he presented a plan of therapy for asthmatic crises and the period immediately following such attacks.

This report was abstracted from the *Boletim do Hospital dos Servidores do Estado.*

Acute pancreatitis—In *Revista paulista de medicina*, M. B. Neto and J. A. Pinotti presented an analysis of 258 patients with acute pancreatitis seen at the Hospital das Clínicas, University of São Paulo Medical School, from April 20, 1950, to December 31, 1957. The pancreas was visualized in 57 patients. Of 28 patients with hemorrhagic necrosis, 22 died; five of 23 patients with edema died, and one of six patients with edema and small areas of hemorrhage died. Not all patients had the complete clinical syn-

(Continued on page A-92)

with a one week course of daily injections

Anergex—1 ml. daily for 6-8 days—usually provides prompt relief that persists for months.

Anergex—a specially prepared botanical extract—is nonspecific in action; it suppresses allergic manifestations *regardless* of the offending allergens. It is not a histamine antagonist, nor does it merely minimize the effects of a single allergen.

Anergex eliminates skin testing, long drawn-out desensitization procedures, and special diets. It has been effective even in patients who failed to respond to other therapeutic measures.

Reports on over 3,000 patients have shown that over 70% derived marked benefit or complete relief following a single short course of Anergex injections. Effective in seasonal and nonseasonal rhinitis (pollens, dust, dander, molds, foods); allergic asthma; asthmatic bronchitis and eczema in children; food sensitivities.

Available: Vials containing 8 ml.—one average treatment course.

WRITE FOR REPRINTS AND LITERATURE

ANERGEX®

the new concept for the treatment of allergic diseases

MULFORD COLLOID LABORATORIES MULFORD PHILADELPHIA 4, PENNSYLVANIA

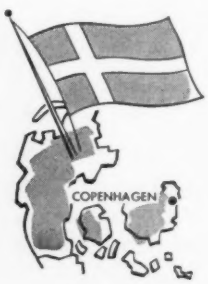
drome of acute pancreatitis; only rarely were all the signs and symptoms present in the same patient. In the majority of cases, laboratory data and roentgenographic examination revealed the correct diagnosis.

Treatment for this condition is conservative except when the diagnosis is in doubt and the patient urgently needs surgical treatment or when obstructive icterus or pancreatic suppuration is present. Clinical therapy consists of fighting shock, relieving pain, reducing intrapancreatic tension, correcting adynamic ileus, maintaining electrolyte balance, and preventing infection in the patient.

Mitral stenosis—In *Anais da Faculdade de medicina de Porto Alegre,* A. G. Mattos presented a discussion of 20 patients who had mitral stenosis without associated regurgitation. In the electrocardiograms of these patients, he found a high percentage of biphasic P waves in V_1 and notched P waves in V_3 and V_4, and he emphasized the incidence of incomplete right bundle-branch block and the low incidence of the QRS complex with aR, qRs, R or Rs aspects (right ventricular overload signal).

The author stressed the semeiologic importance of the electrocardiogram in the diagnosis of mitral stenosis without associated insufficiency, and he showed how the tracing in this disease differs from that in cardiac disease that causes overload of the left atrium, pulmonary circulation and right ventricle in more than two-thirds of the cases.

DENMARK



Listeriosis—Kristine Hauge Kristensen and Ove Jessen reported on 11 patients with listeriosis seen at the Statens Seruminstitut within a period of one year. *Listeria monocytogenes* was found on culture of the spinal fluid in 10 cases, and the disease was diagnosed after postmortem examination of the viscera in one case. Bacteria were detected in a smear of the spinal fluid in only one patient. The following serotypes were found: type 1 in five patients, type 2 in one patient, type 4a in one patient, and type 4b in four patients. There was no indication of an epidemiologic connection among any of these patients.

Three of the 11 patients were newborns. In one of these infants fever, petechiae, cerebral symptoms and purulent meningitis developed on the sixth day of life. In spite of antibiotic therapy, the infant died less than 36 hours after the initial symptoms appeared.

The other eight patients ranged in age from 8 to 69 years. The dominant disease was meningitis or meningo-encephalitis. In most cases the initial symptoms were increasing headache and high fever; often, gastrointestinal or catarrhal symptoms were present for a few days. One patient was admitted first to a surgical ward, because an acute abdominal condition was suspected. In two patients prodromal symptoms, diarrhea, vomiting and a sore throat with fever (in that order) preceded the onset of meningitis by one to two weeks.

During the clinical course of the disease, symptoms of cerebral infection were more predominant than is usual in cases of acute bacterial meningitis. Only two patients had frankly purulent spinal fluid. In the remaining patients only 100 to 900 leukocytes per cubic millimeter were found; 50 to 90 per cent of these cells were mononuclear. The predisposing conditions of leukemia, rectal tumor and puerperium were present in three patients.

In one patient purulent meningitis, which was accompanied by pronounced granulocytopenia with relative mononucleosis in the peripheral blood and by moderate myeloid hyperplasia of the sternal marrow, followed a recurrence of acute tonsillitis. Two patients had moderate peripheral granulocytopenia and relative mononucleosis. In the remaining patients the white blood cell count was normal or showed moderate leukocytosis. In five patients the sternal marrow was histologically normal or revealed slightly increased granulopoiesis. Cold agglutinin titers and results of the Paul-Bunnell test were normal in four patients. All patients received antibiotic therapy; seven recovered in about a week and one patient died.

Wilhelm Frederiksen and Klave Chiewitz described a case of meningo-encephalitis in a 37 year old man. The causal organism was *L. monocytogenes,* serotype 1. Massive doses of antibiotics had no significant effect on the course of the disease. The patient died on the fourth day of illness, after having been comatose for more than two days.

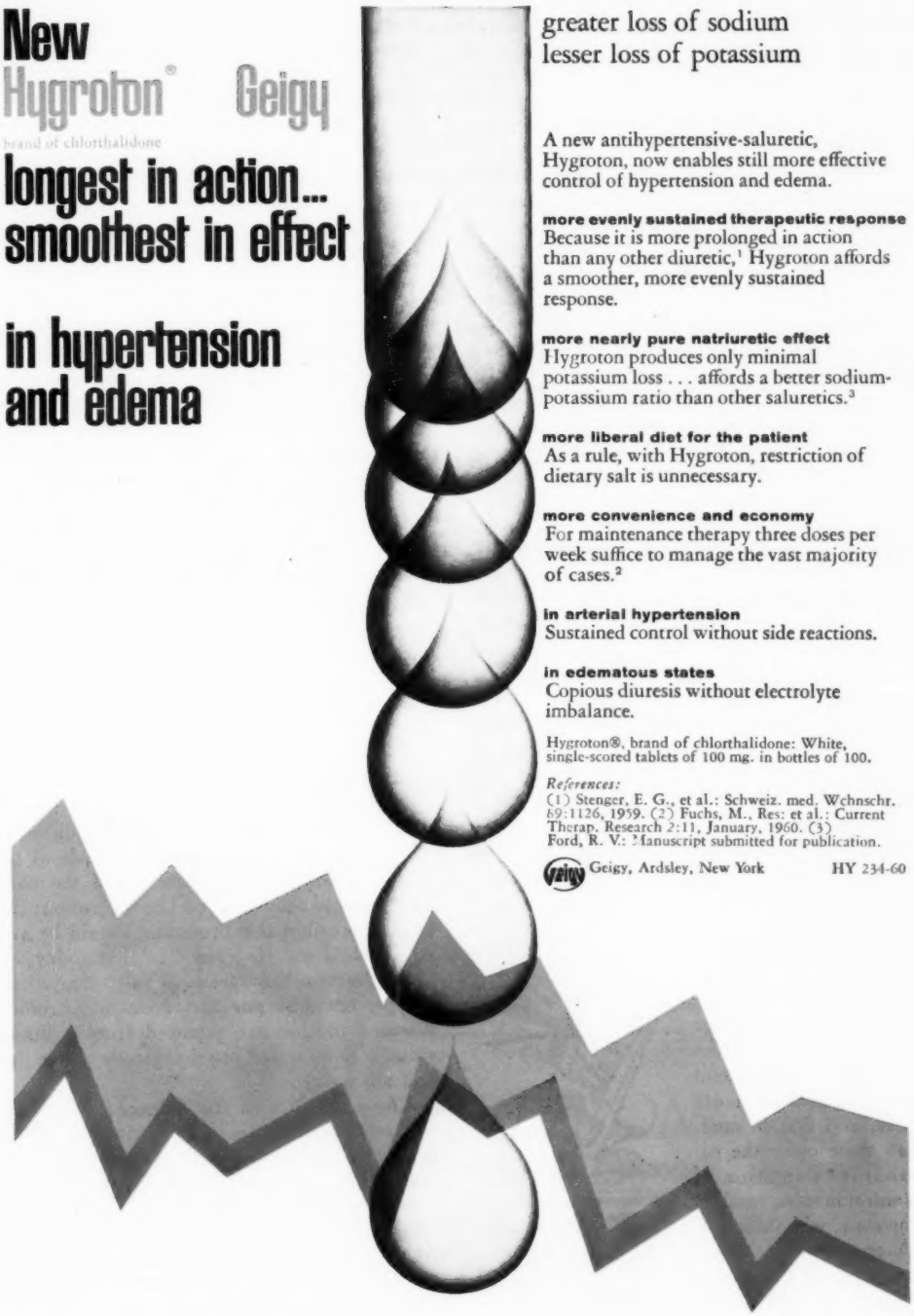
(Continued on page A-94)

New Hygroton® Geigy

brand of chlorthalidone

longest in action... smoothest in effect

in hypertension and edema



greater loss of sodium
lesser loss of potassium

A new antihypertensive-saluretic, Hygroton, now enables still more effective control of hypertension and edema.

more evenly sustained therapeutic response
Because it is more prolonged in action than any other diuretic,[1] Hygroton affords a smoother, more evenly sustained response.

more nearly pure natriuretic effect
Hygroton produces only minimal potassium loss . . . affords a better sodium-potassium ratio than other saluretics.[3]

more liberal diet for the patient
As a rule, with Hygroton, restriction of dietary salt is unnecessary.

more convenience and economy
For maintenance therapy three doses per week suffice to manage the vast majority of cases.[2]

in arterial hypertension
Sustained control without side reactions.

in edematous states
Copious diuresis without electrolyte imbalance.

Hygroton®, brand of chlorthalidone: White, single-scored tablets of 100 mg. in bottles of 100.

References:
(1) Stenger, E. G., et al.: Schweiz. med. Wchnschr. 89:1126, 1959. (2) Fuchs, M., Res: et al.: Current Therap. Research 2:11, January, 1960. (3) Ford, R. V.: Manuscript submitted for publication.

Geigy, Ardsley, New York HY 234-60

Effect of progesterone on aldosterone—In a brief review of the literature, Povl Hempel-Jørgensen and Preben Eilersen discussed the effect of progesterone on mineral metabolism. It was shown that progesterone and spironolactone have an antagonistic effect on aldosterone. This effect is quite probably an expression of "biologic competition."

The authors presented their experience with progesterone therapy in two patients who had cirrhosis of the liver and ascites. The use of diuretics in these patients previously had caused a considerable loss of potassium and a negligible loss of sodium, indicating the presence of secondary hyperaldosteronemia. In this study, the patients were treated with progesterone given alone and in combination with Rontyl and THIOMERIN®. The simultaneous administration of diuretics and progesterone resulted in considerable diuresis, with excretion of chloride and sodium but only a small amount of potassium. Progesterone administered alone had no effect. It is interesting that the initial favorable effect, with excretion of more sodium than potassium, diminished fairly rapidly during prolonged treatment with progesterone; this undoubtedly was due to the compensatory increased production of aldosterone. The authors' preliminary investigations suggested that intermittent treatment with diuretics and progesterone produces the best results.

Methylacetoxyprogesterone, which is an orally administered steroid with a progesteronelike effect, was given to one of these patients. Studies revealed that this agent had no antagonistic effect on aldosterone.

These reports were taken from articles which appeared in *Ugeskrift for laeger.*

ENGLAND

Maxillary sinusitis—It is common knowledge that the maxillary antrum is affected to some extent in many cases of acute coryza, and that in nearly all these cases the catarrhal inflammation of the antral mucosa resolves completely without any form of treatment. In another type of case the main defense mechanism, namely, the ciliary action, has ceased to function. This can occur as the result of the toxins produced by the invading microorganism, but more commonly it is due to the bulk of material accumulated in the antral cavity. In these cases, in addition to the antibiotic therapy necessary to overcome toxemia, mechanical aid to the cilia is required.

Mr. Myles Formby, surgeon to the ear, nose and throat department of University College Hospital, London, discussed this subject in an address at the Royal Society of Medicine. He stated that on more than one occasion antral puncture and simple lavage have effected surprising and lasting improvement in a case considered to be entirely of an allergic nature; and he wondered if such conditions may not in reality be due to a viral infection of the maxillary antrum. In his opinion, surgical intervention in the management of sinus abnormalities should be considered only when nonoperative treatment has been unsuccessful. Conservative measures include removal of any obstruction to normal sinal ventilation, e.g., deformity of the septum or nasal polyps; reduction of the size of the turbinates when they are causing constant blockage of the airway; complete investigation and treatment of any allergy; dental examination and treatment; treatment of any systemic disease; use of the Proetz displacement method; and antral irrigation.

By the process of exclusion the cases requiring surgical intervention are those in which (1) nonsurgical methods have failed; (2) cysts are present in the antrum or an antrochoanal polyp has formed; (3) there is an antro-oral fistula, which is nearly always of dental origin; and (4) there is malignant disease. Mr. Formby believes that in cases in which nonsurgical methods of treating maxillary sinusitis have failed the correct treatment is the Caldwell-Luc operation; however, if possible, this procedure should be avoided in children. He considers that today there is no place for the intranasal antrostomy. Unless polyps, encysted pus and areas of chronically diseased mucosa are removed from a diseased sinus, a normal and physiologically active lining will not re-form.

Chewing gum in the bronchi—The aspiration of foreign bodies into the air passages is an accident which may happen to persons of all ages. Numerous reports in the literature describe a large variety of inhaled objects. Indeed, any object that is held in the mouth may at some time be inhaled, provided it is of a size to pass through the larynx. An unusual foreign body

(Continued on page A-96)

the decorative jar makes a therapeutic difference

The FILIBON jar is a handsome and handy reminder for everyday prenatal nutritional support. You can be sure she will be reminded of her FILIBON-a-day... and that the up-to-the-minute formula covers nutritional defenses throughout pregnancy.

FILIBON provides ferrous fumarate, an iron well-tolerated by even the most easily upset patients. Each small, dry-filled capsule also includes vitamin K and AUTRINIC® Intrinsic Factor Concentrate that enhances, never inhibits, B_{12} absorption. For complete formula see Physicians' Desk Reference, page 697.

LEDERLE LABORATORIES, a Division of AMERICAN CYANAMID COMPANY, Pearl River, N.Y. Lederle

Phosphorus-free FILIBON® Prenatal Capsules Lederle

which can cause death when impacted in a main bronchus is a mass of chewing gum. Drs. F. C. Stallybrass and Rosalie M. Child, pathologists to Manor Hospital, Walsall, have reported in the *British Medical Journal* two deaths due to this cause. Both patients were 62 year old men in good health who died suddenly. It was assumed that death was due to heart disease, but postmortem examination revealed in each case a lump of chewing gum in the right and in the left main bronchus, respectively. There was also some atheroma of the coronary arteries.

Any object temporarily held in the mouth may be inhaled. The longer it remains in the mouth, the greater will be the chance of accidental aspiration; chewing gum is usually held in the mouth very much longer than sweets that dissolve. Perhaps on this account chewing gum is taken more often by people engaged in some physical activity. This association with work is an additional danger, for if involuntary gasping occurs during activity the chance of aspiration is greatly increased. Finally, the habit of adding one piece of gum to another in order to maintain the flavor must be condemned. If gum must be chewed it is better to chew one piece at a time and thus avoid forming a large plug which is capable of obstructing a main bronchus.

Does aspirin cause anemia and peptic ulcer?—Few people would question the value of aspirin in the treatment of rheumatoid arthritis, and carefully controlled trials by the Medical Research Council, the Nuffield Foundation, and the Empire Rheumatism Council have shown little difference between the therapeutic effects of aspirin and cortisone in the long-term management of this disease. However, a number of reports have been published which suggest that aspirin may be an important cause of gastrointestinal bleeding and anemia. In other reports aspirin has been blamed for the exacerbation of symptoms of peptic ulcer, especially hematemesis.

Drs. J. J. R. Duthie and F. D. Baragar of the Rheumatic Diseases Unit, Edinburgh, have published in the *British Medical Journal* an important study of the variations in hemoglobin levels in a large group of patients with rheumatoid arthritis. Most of these patients had been taking aspirin continuously or intermittently in varying doses for a number of years. Duthie and Baragar conclude that the majority of patients with rheumatoid arthritis can tolerate regular doses of aspirin without an increase in anemia. The danger of causing peptic ulceration or of precipitating gastrointestinal hemorrhage appears to have been greatly exaggerated.

FRANCE

Syphilis—In *La Presse médicale*, Dr. Pierre Durel, one of the most esteemed syphilologists in France, reported on syphilitic disease and its two therapeutic phases. He distinguished between the treponemiatic and the cicatricial symptoms of syphilis and stated that this distinction may be made regardless of the chronicity of the disease or whether it is acquired or of congenital origin.

As a general rule, adequate doses of penicillin are effective against the treponemiatic organisms and will cure this phase of the disease almost immediately.

The majority of syphilologists throughout the world concede that nearly all patients are cured very quickly. Some authorities administer 5 to 6 million units of a long-acting penicillin, such as PAM or benzathine penicillin G, while others prescribe bismuth in addition to penicillin. Durel advocated the use of penicillin alone. He cited the absence of resistant strains in the rabbit and pointed out that endemic syphilis has disappeared in underdeveloped countries where only a single shot of penicillin is usually given. He stated that cures have been obtained with only 300,000 units of penicillin and that tertiary, neural and aortic forms of syphilis have disappeared among patients in hospitals.

However, contrary to these clinical facts, positive serologic findings persist in about 10 per cent of cases. Durel does not believe that such cases are due to the evolutive, threatening character of the infection; nor does he think that the proportion of persons affected has any relationship either to the dosage of penicillin (which varies from 2.4 to 20 million units) or to the supplementary treatment with bismuth. He considers that this occurrence is due to a persistent humoral reaction in the patient who continues to produce antibodies after the disease has already been suppressed.

Superinfections occur more frequently after treatment with penicillin alone, which protects the patient for only a few weeks, than they do

when bismuth is given. Successive serial treatments with the latter establish a bismuth depot which is effective for years and which neutralizes any intercurrent reinfection.

In some patients with chronic syphilis, complications resulting from destruction and sclerosis of the tissues may develop immediately after the treponemiatic phase. In other patients, complications in which the cicatricial process is delayed, such as tabes in which the serologic findings are negative, aortitis, and possibly even aneurysms of the aorta, may develop very slowly after the treponematosis has been cured. Allergic gummatous complications, which are related to the action of a new "crop" of treponemas on an altered and sensitized area, also may occur; these complications are comparable to the Koch phenomenon. The new treponemas may be endogenous (in patients who have not had sufficient treatment) or exogenous (as the result of a superinfection).

It may be concluded that when the infection has been treated correctly patients with chronic syphilis do not require further specific treatment. However, the physician often does not know whether proper treatment has been given previously, and he has no criteria for a cure. The patient's mental attitude influences him to give treatment, and his own cautiousness requires that potent serial treatment with penicillin be given. Durel believes that treponematosis, if it has persisted, is cured immediately by penicillin.

The Jarisch-Herxheimer reaction should be watched for; however, it can be avoided by attacking the syphilis progressively and by using antihistamines, although these drugs may be dangerous to babies. A "therapeutic paradox" also may occur, in which the patient, although cured of syphilis, continues to have visceral complications such as infarction or cardiac or renal failure, or both.

Durel recommended that penicillin should not be given, even with great caution, to persons allergic to it. In its place, he advocated administering 2 gm. tetracycline or 3 gm. spiramycin, supplemented with bismuth at the end of two weeks.

Nonspecific therapy, including the use of cyanide, malariotherapy and delta-cortisone, is indicated in patients with cicatricial complications such as tabes, optic neuritis, aortic ectasias and cirrhosis of the liver. Antisyphilitic medications are useless in these cases, since treponemiatic organisms are no longer present.

JAPAN

Leukemia—In *Acta haematologica Japonica,* Dr. Gyoichi Wakisaka, professor of medicine, Kyoto Imperial University Faculty of Medicine, discussed clinical and statistical research on leukemia. According to the vital statistics of Japan, the annual death rate from leukemia per 100,000 population rose from 0.51 (257 deaths) in 1910 to 1.4 (969 deaths) in 1935. From 1935 to 1948 the death rate remained nearly constant, but thereafter it increased steadily to 2.3 (2,038 deaths) in 1955. The mortality from leukemia per 10,000 deaths from all causes rose from 2.41 in 1910 to 8.3 in 1935 and to 29.4 in 1955. The incidence of leukemia is still lower in Japan than in most other countries; however, in Hiroshima and Nagasaki a higher incidence has been observed among the survivors of the atomic bomb.

During the period 1935 to 1955, more men than women died annually from leukemia; the death rate in men was from 1.26 to 1.56 times greater than that in women. This same pattern has been observed in other countries. The age distribution curve of the death rate from leukemia in 1951 and 1955, charted by quinquennia, showed three peaks, namely, in children up to four years of age and in persons from 35 to 44 and from 55 to 69 years old. The greatest increase in the mortality occurred in the oldest age group. The age distribution was practically identical for both sexes.

Wakisaka also studied 927 hospitalized patients, particularly investigating cellular types, heredity, history, symptoms, physical signs, hematologic and laboratory findings, response to treatment, and length of survival. Of the 927 patients, 604 had an acute or a subacute form of leukemia. Acute granulocytic leukemia was present in 41.4 per cent of the patients, acute lymphocytic leukemia in 9.5 per cent, acute monocytic leukemia in 8.9 per cent, acute leukemia of an unknown type in 5.5 per cent, chronic granulocytic leukemia in 28.8 per cent, chronic lymphocytic leukemia in 2.7 per cent, and other types of leukemia in 3.2 per cent. Leukemia was found in 0.5 per cent of the family histories and malignant neoplasms in 10.6 per cent. Leukemia had

(Continued on page A-98)

developed in 21 of 563 patients following exposure to the atomic bomb.

Influence of high altitude—Dr. Toshiro Oda, a professor at Osaka Imperial University Medical Faculty, has studied the influence of high altitude on the constituents of human blood. Results of his investigation have been published in the *Journal of the Japanese Society of Internal Medicine*. The following changes were observed in subjects who climbed the Japanese Alps: (1) slight fluctuation in the number of red cells in the early stage of the test, with a subsequent increase in the terminal stage; (2) a decrease in the amount of hemoglobin in the early stage, followed by a return to normal levels; (3) marked decrease of eosinophils in the initial stage, with recovery in the terminal stage in most of the examined subjects. The hematocrit reading showed an increased value in the terminal stage, and there was an increased volume of blood cells. There was no marked change in the concentration of creatinine in the blood. One-half of the subjects initially had slight albuminuria, which soon subsided.

Electrophoresis was used to analyze the serum proteins of 10 persons who traveled by bus to Mount Norikura, an altitude 2,740 meters above sea level. These persons stayed in the research laboratory and did no physical labor during the test period. Serum proteins in these subjects decreased slightly immediately following the trip, but returned to a constant value one week later. The albumin fraction and the albumin-globulin ratio increased in some of this group at the beginning of the study, decreased on the third and fifth days, and then returned to the initial value. The gamma-globulin fraction increased distinctly on the fifth day after the trip, even though there was no significant change in the alpha-globulin and beta-globulin fractions.

Thalassemia—A case of thalassemia has been reported for the first time in Japan by Dr. Akira Sakamoto and co-workers of the department of pediatrics, Nagoya Medical College. The patient was an 11 year old Japanese boy of consanguineous parents. His stature was that of a normal seven year old boy, and his nose was short with a depressed bridge. The disease was diagnosed on the basis of the characteristic skull change that is seen in Cooley's anemia in which the hair "stands on end."

The patient had had hepatosplenomegaly without any bleeding tendency since he had been six months old. On examination, the liver and spleen were palpable about 10 cm. below the costal margin. Laboratory data showed that the red blood cell count ranged from 4.6 to 1.79 million, hemoglobin from 34 to 16 per cent, platelet count from 110,000 to 64,000, white blood cell count from 4000 to 3400; the differential counts were normal. Normoblasts varied from 4 to 14 per 200 red cells. The erythrocytes stained colorless with some target cells. Examination of the bone marrow showed increased erythrocytopoiesis. Determination of osmotic fragility revealed that the maximal resistance of the red cells ranged from 0.36 to 0.32 per cent and the minimal resistance was 0.44 per cent. Biochemical tests disclosed the presence of 83 μg. serum iron per 100 ml. and 3.1 per cent fetal hemoglobin.

This report is based on an article in *Acta haematologica Japonica*.

SPAIN

Treatment of poliomyelitis—About 200 patients with serious cases of poliomyelitis have been treated during the past two years at the Niño Jesús Hospital in Madrid. The number of patients now under treatment has dropped to an estimated 25 per cent of this figure. Some 60 per cent of patients recover from the disease. Under Dr. Olaizola's direction, 8000 persons have been vaccinated against poliomyelitis at this hospital; records show that not one of them has contracted the disease. The use of iron lungs has proved to be the most effective treatment.

The new poliomyelitis pavilion in the Hospital del Rey was opened recently in a ceremony presided over by the Minister of the Interior. The pavilion houses 132 children who are recuperating from polio. Facilities for treatment include x-ray units, an electrocardiograph and other electrodynamic apparatus, pools, a gymnasium, and seven iron lungs. Two of the iron lungs are for adults and five are for children; respirators with positive and negative pressure also are used. Paralysis in the arms and legs is treated with hot wet packs, and braces are used to prevent deformities. Patients with paralysis of the spinal or abdominal muscles must remain almost constantly in bed; they are held in position with plaster

(Continued on page A-100)

from carcinomatosis
to carsickness

"To those patients who had multiple metastases and metastatic lesions, Tigan was truly a godsend, enabling them to continue treatments and obtain relief . . . not obtainable in any other non-surgical way."[1] Successful in some of the most challenging conditions, such as radiation[1,2] or nitrogen mustard therapy,[3-5] Tigan is equally effective in all other situations calling for the prevention or control of nausea and vomiting. Travel sickness, pregnancy and gastrointestinal disorders are among the leading indications for Tigan. Three convenient forms: Tigan Capsules—100 mg, blue and white • Tigan Ampuls—2 cc (100 mg/cc) • Tigan Suppositories—200 mg.

no special precautions
no known contraindications

Tigan

safely controls the entire range of emetic situations

References: 1. J. A. Lucinian and R. H. Bohn, paper read at Colloquium on The Pharmacological and Clinical Aspects of Tigan, New York City, May 15, 1959. 2. H. E. Davis, Discussant, *ibid.* 3. W. B. Abrams, I. Roseff, J. Kaufman, L. M. Goldman and A. Bernstein, *New York J. Med.*, *59*:4217, 1959. 4. I. Roseff, W. B. Abrams, J. Kaufman, L. Goldman and A. Bernstein, *J. Newark Beth Israel Hosp.*, *9*:189, 1958. 5. B. I. Shnider and G. L. Gold, paper read at Colloquium on The Pharmacological and Clinical Aspects of Tigan, New York City, May 15, 1959. 6. M. W. Goldberg, *ibid.* 7. O. C. Brandman, *ibid.* 8. D. W. Molander, *ibid.* 9. W. S. Derrick, *ibid.* 10. B. Wolfson and F. F. Foldes, *ibid.* 11. W. K. Gauthier, Discussant, *ibid.* 12. L. McLaughlin, *ibid.* 13. W. Schallek, G. A. Heise, E. F. Keith and R. E. Bagdon, *J. Pharmacol. & Exper. Therap.*, *126*:270, 1959. 14. Reports on file, Roche Laboratories. 15. Personal communications.

ROCHE LABORATORIES
Division of Hoffmann-La Roche Inc. Nutley 10, N. J.

TIGAN® Hydrochloride—4-(2-dimethylaminoethoxy)-N-(3,4,5-trimethoxybenzoyl) benzylamine hydrochloride

casts until the worst phase of the disease is past.

The National Poliomyelitis Service has 130 beds, including cribs and half-size and adult beds; there are eight cribs in a room. The children, most of whom are less than three years of age, are under the constant care of a nurse. Eleven nurses, trained in physiotherapy at the Universidad Central de España Facultad de Medicina of Madrid, are in charge of treatments.

After the first month of their illness, patients in the poliomyelitis pavilion are given a muscular balance test to determine the condition of each muscle; results are judged according to international classifications numbering from one to five, and are recorded on the patient's personal history chart. Each nurse takes charge of 10 children, carrying out the special exercises prescribed for them by the attending physician. An orthopedic specialist directs the exercises of patients wearing plaster casts.

As a result of treatments carried out in this pavilion, 80 per cent of the children return home completely cured, and 20 per cent are fitted with an orthopedic apparatus enabling them to walk by themselves.

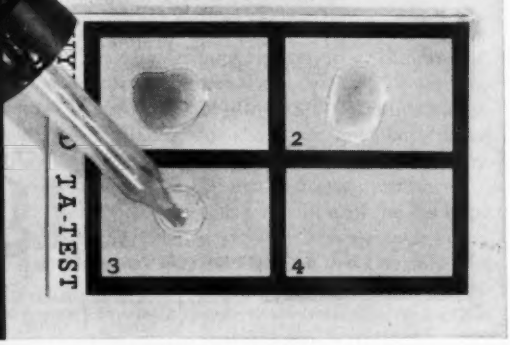
Health Control Center—The country's first Health Control Center has recently been opened in Valencia. This center was organized by the Spanish Cancer Society in order to furnish gratuitous medical examinations and analyses to the public.

Detection of any noncancerous manifestation of disease is communicated to the individual being examined, and recommendations for treatment are given. When cancer is discovered, the patient remains under the care of the Provincial Board, unless he has ample personal means to pay for proper treatment. The Board sees that the patient is treated either in his home or in a sanatorium or clinic under its direction. By providing a means for early detection of cancer, the Health Control Center will greatly aid the activities of the Spanish Cancer Society.

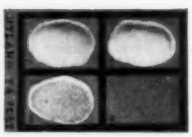
At the opening of the Center, Dr. Juan Bosch Marin, Chief of the National Puericulture Program, spoke of the great importance of the work done at the Center in checking general health conditions. This type of program has already been carried out for tuberculosis, leprosy and trachoma, and is part of the general organization of the Spanish Puericulture Program. Dr. Marin stated that approximately 17,000 persons in Spain die annually from cancer and that about 30,000 persons have this disease.

TA-TEST*

RAPID SLIDE TEST FOR DETECTION OF THYROGLOBULIN AUTOPRECIPITIN ASSOCIATED WITH HASHIMOTO'S DISEASE



TA-TEST provides an important new time-saving procedure in diagnosis of thyroid disease. It speedily detects thyroglobulin autoprecipitin, associated with Hashimoto's Disease (chronic lymphoid thyroiditis) and primary myxedema. Since both of these conditions are treated medically, rather than surgically, the diagnostic helpfulness of this new screening test is obvious. The test is simple to perform and requires only two drops of patient's serum. Results are then read within two to three minutes. TA-TEST is supplied in compact 20-test kits containing reagent, diluent, control serum and glass slide. List No. 90-100



1. Negative specimen, undiluted
2. Negative specimen, diluted
3. Positive control

*Trademark of Hyland Laboratories

HYLAND LABORATORIES

4501 Colorado Blvd.
Los Angeles 39, Calif.
160 Lockwood Ave., Yonkers, N.Y.

Hyland

DR. ARTHUR G. SULLIVAN MEMORIAL LECTURE*

Carcinoma of the Stomach

SAMUEL F. MARSHALL†

Lahey Clinic, Boston

Carcinoma of the stomach is not considered a disease with a hopeless prognosis.

Great progress has been made in treating precursors of gastric cancer, including atrophic gastritis and polyps.

Patients with minor digestive symptoms, epigastric distress, anorexia and slight weight loss should be examined carefully to rule out the possibility of carcinoma.

Operation must be performed early in the course of the disease.

Present-day radical procedures include a wide excision, with removal of the omentum and all avenues of spread.

THIS is the Arthur G. Sullivan lecture, given in commemoration of Dr. Sullivan's untiring efforts in behalf of this great organization and his many significant contributions to it.

SAMUEL F. MARSHALL

I would like to approach the problem of carcinomas of the stomach from a more hopeful attitude than in the past. We have made definite progress in the treatment of carcinoma of the stomach. Much, of course, depends on its early diagnosis. That is a trite statement, but after reviewing the literature and our own experience the consensus is that if the diagnosis can be made within three months of the onset of minor digestive symptoms, something can be done to improve the results of treatment of carcinoma of the stomach. Carcinoma has certain biologic characteristics that influence the survival rate, but what those characteristics are I am not sure. I thought that we had gained something from histologic study but after reviewing the pathologic findings in our series of cases, we found nothing in the microscopic anatomy that helped us to determine the survival rate.

Cancer of the stomach accounts for about 10 to 15 per cent of all deaths from malignant

*Established by the Interstate Postgraduate Medical Association in 1957 in memory of Dr. Arthur G. Sullivan, who served as Managing Director for the 17 years preceding his death in 1954. Dr. Sullivan was also Managing Editor of POSTGRADUATE MEDICINE from its inception until his death.

†Department of Surgery, Lahey Clinic, Boston, Massachusetts.

Presented before the forty-fourth annual Assembly of the Interstate Postgraduate Medical Association at Chicago.

disease. We recently studied all of our cases of carcinoma of the stomach for a period of 23 years, from 1932 through 1954, and were able to determine accurately what became of all but three of that group of 1,708 patients. We now have some completely new data that I would like to bring to your attention.

The frequency of carcinoma of the stomach has decreased over a period of 10 years. In 1948, carcinoma of the stomach accounted for 13.3 per cent of all deaths from cancer. In 1957, that figure was 8.5 per cent, a significant drop since the total number of deaths from all forms of cancer has increased, according to the Bureau of Vital Statistics. Cancer of the stomach usually occurs in older individuals—90 to 92 per cent of our patients were past the age of 50. The decrease in deaths from cancer of the stomach is surprising since life expectancy has increased to about 70 years. The sex ratio is two males to one female.

The ratio of deaths from cancer of the stomach to total deaths from all forms of cancer varies over the world. Tazaki reported that, in Chile, cancer of the stomach accounts for 49.3 per cent of the total deaths from all forms of cancer. In Japan that figure is 58.7 per cent —more than half of those who die from cancer die of cancer of the stomach.

Considerable evidence is found in the literature to indicate that cancer did occur in antiquity. Hippocrates spoke of gastric tumors. Sigerist stated that although the records of cancer of the soft parts are scant, cancer must have occurred in the early Egyptian days. He has also told us that even though cancer has never been found in an Egyptian mummy, very few have been examined for soft tissue tumors, so it is difficult to tell much about it.

Knowledge of the etiology of cancer of the stomach would be helpful, but the causative factors are not known. Food, alcohol and tobacco may be factors, and the high incidence of the disease in Chile and Japan indicates that they may have something to do with it. There is no definite evidence, however, that food, alcohol and tobacco promote gastric cancer.

The greatest progress has been made by adequate treatment of some of the precursors of cancer. I will mention only a few. Atrophic gastritis plays a great part in the development of carcinoma. Gastric ulcer need not be discussed because the literature indicates that 10 to 20 per cent of gastric ulcers are malignant when operation is performed—16.7 per cent in our experience. Polyps are precursors of cancer; 30 per cent of them have proved to be malignant. The incidence of gastric cancer in patients with pernicious anemia is five or six times that in patients who do not have pernicious anemia. Zamcheck and his coworkers at the Boston City Hospital studied 1,222 patients with pernicious anemia and found that 10 per cent had gastric cancer. They recommended routine screening tests for patients with pernicious anemia to rule out cancer. We believe gastroscopic examination should be included, because adenomatous polyps may be present and malignant degeneration of polyps often develops in patients with pernicious anemia.

One great difficulty in the study of gastric carcinoma is the lack of uniformity of pathologic classifications. Borrman's classification takes into consideration the gross characteristics and the size of the tumor, but surgeons and pathologists differ in their interpretation of the type of tumor. The surgeon needs to know whether lymphatic metastases and vascular involvement have occurred in order that he may excise all avenues of spread of cancer. Therefore, the histologic method is of greater value to him, because by using it he can determine which type of tumor will metastasize.

The progress that has been made in the treatment of gastric cancer is of particular interest, and we do not have to go back many years. At the beginning of the twentieth century, Bloodgood of Johns Hopkins had done a great deal of work on carcinoma of the stomach. He found that from 1889 to 1915 the condition was operable in only 30 per cent of cases at the time the patient was seen; cure was not obtained in 98 per cent. Bloodgood reported that only 30 gastric resections had been performed in 25 years, with three patients surviving five years. In 1914, Friedenwald reported on 1000 cases collected from

the literature; resection was successful in nine cases and only one of the 1000 patients lived 15 years. By glancing through some of the older textbooks one can see that the mortality rate was much higher and the survival rate much lower than today. DaCosta stated that resection for carcinoma of the stomach is associated with a very high mortality—from 25 to 30 per cent. He said that he had never performed a total gastrectomy and saw very little need for it. Moynihan, in 1926, reported on two total gastrectomies; with all of his experience he had performed only two total gastrectomies to that date.

The changes in the surgical treatment of carcinoma of the stomach that have taken place in a period of 30 to 40 years are interesting. Today a radical procedure for carcinoma of the stomach includes a wide excision, with removal of the omentum and all avenues of spread—the lymphatic and vascular vessels. Bloodgood mentioned the common mistake that the surgeon made resecting too much of the stomach; he said that if one took too wide a margin of normal tissue, a Billroth I could not be performed. Another thing that impressed me was that none of the early surgeons (Moynihan, Richardson and Finney) excised the omentum. Bloodgood stated that if the tumor involved the omentum or the lymph nodes of the stomach, operation was useless because cure was never obtained. We must remember also that x-rays were not discovered by Röntgen until 1895 and were not used as a method of diagnosis until 1901. Thus, in this large series of cases, the diagnosis had to be made chiefly by the clinical findings, and so the majority of patients who came to the surgeon in the early days were beyond any surgical help.

The first successful resection for cancer was performed by Billroth in 1881, but numerous attempts had been made prior to that time. Jules Pean tried to resect a stomach in 1879 and the following year Rydygier attempted removal but failed. Many such experiments had been carried out on animals before that time, and the results indicated that animals could live without a great portion of the stomach. It is largely due to Billroth's efforts in 1881 and 1885 when the Billroth I and II procedures were developed that most of our operations today are successful; most of the procedures employed today are modifications of the Billroth I and the Billroth II.

American surgeons had a great part in the development of gastric surgery. For instance, in 1895 Welch noted that 25 different surgeons had performed 37 operations and 27 of the patients died. He could see no reason to believe that cancer of the stomach could ever be cured. When I was in Baltimore in 1924 I heard Finney say he had never seen a cancer of the stomach cured; at that time the outlook was very black. The Mayos did much to improve the technic of gastric resection and to lower the mortality rate. In 1919, they reported a series of 736 resections over a period of 23 years, with a mortality rate of 13.7 per cent. That is a reduction of the mortality rate from 25, 40 and 50 per cent in 1897 to 13.7 per cent in 1919.

The mortality rate has decreased almost precipitously. Today the surgeon and internist are aware of the frequency of cancer of the stomach, but are they aware of the possibility that these patients may survive for long periods and that the operative risk is slight? For instance, at the Lahey Clinic the mortality rate with all operative procedures (including palliative resections, exploratory operations and curative resections) for gastric carcinoma was 21.7 per cent in the period 1930 to 1935 and 5.7 per cent in the period from 1950 to 1955. At present the mortality rate associated with partial resection is 3.2 per cent and with total gastrectomy it is 7 per cent. We are operating on a higher percentage of patients. They come to us earlier, but not early enough.

I should like to discuss diagnosis briefly. We do not wait until advanced symptoms of gastric carcinoma are present. Minor digestive symptoms, epigastric distress, anorexia and slight weight loss should arouse suspicion, and all patients with such symptoms should be examined carefully with all available diagnostic methods to rule out carcinoma. Moynihan said that the mortality rate associated with any "operation of inquiry" is almost zero. In many cases the decision to operate must be

based solely on suspicion; otherwise, operation would be deferred until the cancer is advanced and inoperable.

The development of total gastrectomy is very interesting. The first total gastrectomy was performed in 1884 by Connors of Cincinnati, but the patient died on the operating table. The first successful total gastrectomy was carried out by Schlatter of Zurich in 1897. The next four successful total gastrectomies were performed in rapid succession by Americans: Brigham of San Francisco, Richardson of Boston (the operation lasted one hour, which compares favorably with the operative time today), MacDonald of San Francisco (time of this operation was 90 minutes), and Harvie, a gynecologist in Troy, New York (his operating time was even less). These four patients lived for some time. The operative reports are amusing—MacDonald's patient was fed peptonized milk and whiskey every hour, starting the day after operation. The early surgeons were not deficient in technical procedures and ability or remiss in their treatment. Actually, they were superb surgeons and worked under conditions that we would not think of accepting today.

In our study of carcinoma of the stomach, the 1,708 cases were grouped according to the length of time symptoms had been present. Only 358 patients had had symptoms for less than three months. Of the 1,350 cases in which symptoms had been present for three months or more, the patient delayed consulting a physician in 506 cases; in 680 cases the family physician was responsible because he failed to obtain x-ray and laboratory studies; and in 164 cases we deferred examination for more than three months after symptoms began. This study emphasized to us that we must consider minor gastric symptoms carefully and obtain laboratory studies early if carcinoma of the stomach is to be ruled out. In many cases an exploratory operation should be performed if an x-ray defect is seen in the stomach which cannot be identified. In view of the low mortality, exploratory operation is justifiable.

A palpable mass was present in 30 per cent; about one-third of these patients could be operated on but none survived five years.

A diagnosis was established at operation in 1,666 of the 1,708 patients; the tumor was resectable in 856 and nonresectable in 810. Thus the resectability rate was 51.4 per cent —about the same as it has been throughout the country in the last eight years. Resectability does not mean that curative resections were performed. In a curative resection, all evidence of the tumor is removed; that was possible in 652 of 1,666 cases, or 39.1 per cent.

Real progress has been made in selecting cases for operation. Resectability has increased from 45.5 per cent in 1932 to 59.2 per cent in 1954, but the rate for curative resections has increased in these same years from 38.6 to 41.5 per cent. Thus curative resection is possible for nearly half of the patients who come to operation.

What has happened to those patients who had palliative resections? Of the total group of 1,708 patients, 11.4 per cent lived five years or more. Of the patients who had some type of operation—exploratory, palliative or curative resections—22.8 per cent were alive five years later. Twelve patients who had palliative resection survived for five years, so palliative resections are worthwhile.

In this group of 1,708 cases of gastric cancer the five year survival after curative resection increased from 15.4 per cent in 1932 to 39.5 per cent in 1954.

Tremendous progress has been made in the treatment of carcinoma of the stomach; it is by no means a hopeless disease. We must remember that these patients can be cured, and we must operate early in the course of the disease. Treatment is delayed in most cases because of delay in obtaining x-ray and laboratory studies, because of the ignorance of the general public regarding specific problems in gastric distress, and because the importance of minor indigestion is not recognized. If we consider these factors, we can increase the survival rate, operate on more of these patients, and perform more radical operations with a steadily decreasing mortality rate.

The Clinical Usefulness of Orally Administered Hypoglycemic Agents

GEORGE J. HAMWI* AND THOMAS G. SKILLMAN†

Ohio State University Health Center, Columbus

The three orally administered hypoglycemic agents currently available in the United States are tolbutamide, chlorpropamide and phenformin.

When effective, these compounds reduce blood glucose levels, quantitatively reduce glycosuria, and reduce the net hepatic glucose output.

Tolbutamide appears to be effective in older patients with mild diabetes; chlorpropamide seems the treatment of choice in more severe cases. Phenformin may be used alone or as an adjunct to insulin therapy. Generally, side effects are sufficiently mild to be counteracted by cessation or reduced dosage of the drugs. In some cases, however, severe and irreversible damage has occurred.

GEORGE J. HAMWI

DURING the past five years the recent upsurge of interest in the field of diabetes has become apparent to everyone. The general acceptance of the orally administered agents in the treatment of diabetes has resulted in a more convenient means of therapy for the patient. The major impetus, however, has been to stimulate a resurgence of thinking regarding the pathophysiology of diabetes. As a consequence, these orally administered agents have provided a potent stimulus to our understanding of what goes on and what goes wrong in diabetes.

When one considers the clinical usage of a new group of drugs, a series of questions must logically be answered prior to their use. Such a series might include the following: What is their history or background? What are they? How do they work? What do they do? What does pharmacologic study reveal? When

*Professor of Medicine and Chief; †Assistant Professor of Medicine, Division of Endocrinology and Metabolism, Ohio State University Health Center, Columbus, Ohio.

Presented by Dr. Hamwi before the forty-fourth annual Assembly of the Interstate Postgraduate Medical Association at Chicago.

TABLE 1

INTRODUCTION OF ORALLY ADMINISTERED HYPOGLYCEMIC AGENTS

COMPOUND	YEAR INTRODUCED
Synthalin	1926
Blueberry extract	1927
Sulfamidothiazol	1942
Carbutamide	1955
Tolbutamide	1956
Chlorpropamide	1957
Metahexamide	1957
Phenformin	1957

TABLE 2

PHYSIOLOGIC EFFECTS OF ORALLY ADMINISTERED HYPOGLYCEMIC AGENTS

AGENT	PHYSIOLOGIC EFFECTS
Tolbutamide and chlorpropamide	Lower blood and urine glucose Increase liver glycogen Decrease liver glucose output Decrease plasma nonesterified fatty acids
Phenformin	Lowers blood and urine glucose Decreases liver glycogen Elevates blood lactate and pyruvate

are they used? What are their advantages and disadvantages? How are they used? Do they produce toxicity? The aim of our discussion is to consider each of these queries briefly, with the hope of providing an over-all survey of these compounds to permit their optimal clinical utilization in the treatment of patients with diabetes mellitus.

History of Hypoglycemic Agents

The concept of an oral route for the administration of a drug to control hyperglycemia is, of course, not new. Table 1 lists the historical relationship of some of these compounds. Excellent reviews which cover the history of oral therapy are found in the literature.[1,2] In 1926, only five years after the introduction of insulin, synthalin, a chemical derivative of guanidine, received rather widespread use as an oral hypoglycemic agent, but its popularity was short-lived because of reports that it induced liver damage.[3] In the next year, Allen[4] reported that myrtillin, an extract of blueberries, was capable of lowering blood sugar, but again interest in this drug was brief because of its very mild hypoglycemic effect.

The reports of the French investigators Loubatieres and associates[5] and Janbon and co-workers[6] in 1942, describing the accidental induction of hypoglycemia by the administration of a number of different sulfonamides, escaped global recognition; it was not until the report of the Germans Franke and Fuchs[7] in 1955 that much interest was given to this problem. The clinical availability of the sulfonylureas quickly followed: carbutamide in 1955,[8] tolbutamide in 1956,[9] chlorpropamide in 1957,[10] and metahexamide in 1957.[11] Phenformin, a diguanide unrelated to the sulfonylureas, also was introduced in 1957.[12] Although each of these compounds has had an extensive clinical trial, today only three are available commercially in the United States. Tolbutamide is sold by the Upjohn Company under the trade name of ORINASE®. Chlorpropamide is available from the Pfizer Laboratories as DIABINESE®. Phenformin has been marketed by the U.S. Vitamin Corporation as DBI®. Carbutamide is available in Europe and South America as NADISAN®, but was not distributed commercially in the United States by Eli Lilly and Company because of a somewhat high incidence of untoward toxic effects which occurred during its experimental usage.[8] A similar fate befell metahexamide.

Discussion in this paper will be limited to the three currently available compounds tolbutamide, chlorpropamide and phenformin.

What Are They?

Figure 1 lists the various chemical formulas, chemical names, trade names and sources of these drugs. The first two compounds are sulfonylureas. Chemically, tolbutamide differs from chlorpropamide in two ways. At the para position on the benzene ring, tolbutamide possesses a methyl group while chlorpropamide contains a chloride. The aryl side chain is made up of four carbons (butyl) in tolbutamide and three carbons (propyl) in chlorpropamide. Phenformin (phenethylbiguanide) is a diguanide and differs completely from the sulfonylureas in its chemical configuration.

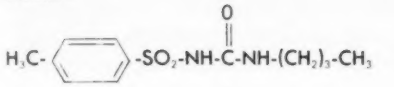
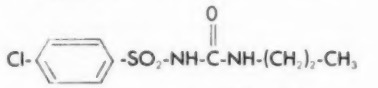
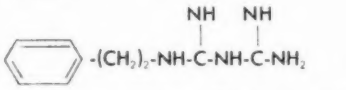
Formula	Chemical Name	Trade Name	Manufacturer
	Tolbutamide	ORINASE®	The Upjohn Company
	Chlorpropamide	DIABINESE®	Chas. Pfizer & Co., Inc.
	Phenformin	DBI®	U. S. Vitamin Corporation

FIGURE 1. The currently available orally administered hypoglycemic agents.

How Do They Work?

Although the mechanism of the hypoglycemic effect of the sulfonylurea compounds is not completely understood, it appears likely that there are two basic mechanisms: (1) stimulation of the beta cells to increase the formation or the release, or both, of insulin[13] and (2) suppression of glucose release from the liver,[14] possibly an insulin effect. The hypoglycemic effect of phenformin does not appear to be mediated by insulin.[15] In our laboratory, in vitro studies have shown that phenformin inhibits cellular aerobic oxidation by inhibiting the transport of electrons within the high-energy phosphate system.[16] This mode of action has not been demonstrated in vivo, and therefore, the actual physiologic mechanism by which phenformin lowers blood sugar must remain speculative.

What Do They Do?

The metabolic effects of the sulfonylureas tolbutamide and chlorpropamide are, in most respects, similar to those of insulin (table 2). When effective, these compounds reduce blood glucose levels and, as a sequence to this, quantitatively reduce glycosuria. They also increase the glycogen content of the liver and reduce the net hepatic glucose output.[17] The demonstration that these compounds cause a decrease in the concentration of free fatty acids in the plasma may be taken as proof that glucose utilization is increased.[18]

Phenformin causes a decrease in plasma and urine glucose concentration in the diabetic human and in pancreatectomized animals.[18] In animals this compound has been shown to decrease liver glycogen content as well,[19] and in both man and animals it causes an elevation of blood lactate and pyruvate levels.[20] Phenformin has also been shown to decrease free fatty acids in the dog.[21]

Pharmacology

Table 3 shows a comparison of the compounds with respect to dose, effective blood level, half-life, metabolism and excretion. There is a rather critical relationship between the magnitude of the dose, the frequency of

TABLE 3

PHARMACOLOGY OF ORALLY ADMINISTERED HYPOGLYCEMIC AGENTS

AGENT	DAILY DOSE (GM.)	EFFECTIVE BLOOD LEVEL (MG. PER CENT)	HALF-LIFE (HOURS)	METABOLISM	EXCRETION
Tolbutamide	1.0-2.0	8-18	4	Methyl group oxidized by liver	Kidney
Chlorpropamide	0.1-0.5	8-18	30-34	Probably not metabolized	Kidney
Phenformin	0.05-0.20	Unknown	Unknown	Unknown	Probably kidney

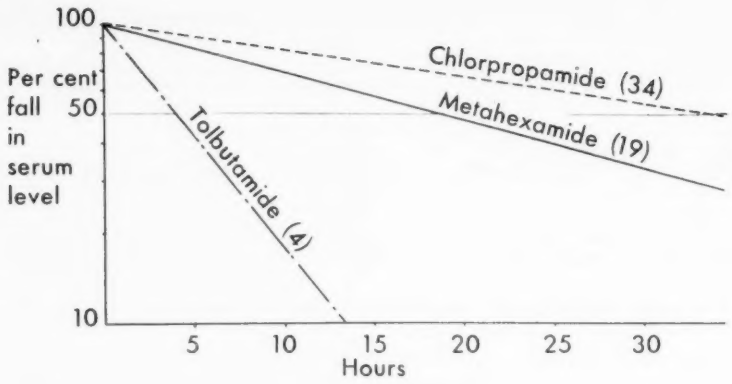


FIGURE 2. Comparative half-lives of orally administered hypoglycemic agents.

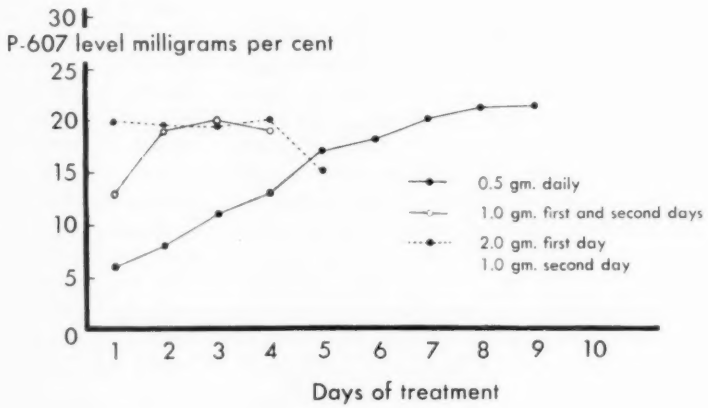


FIGURE 3. Illustration of the gradual increase in chlorpropamide (P-607) blood level during constant daily dosage.

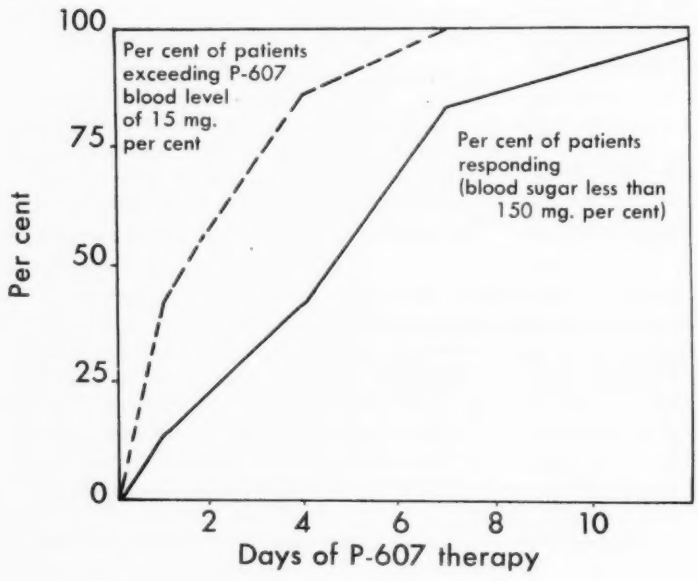


FIGURE 4. Illustration of delay in hypoglycemic response to chlorpropamide despite early achievement of therapeutic blood levels.

administration, and the half-life of the two sulfonylureas. Because the liver is able to oxidize the methyl group of tolbutamide to an intermediary compound which is devoid of hypoglycemic activity, the effective half-life (time needed for a given blood concentration to fall 50 per cent) is short. The presence of the chloride in the molecule of chlorpropamide causes this drug to resist degradation so that it is excreted intact and has a long half-life (30 to 34 hours). Since the blood levels necessary for hypoglycemic action of these two drugs are similar, the daily dose of tolbutamide is greater (4 to 10 times) than that of chlorpropamide. As a result, tolbutamide frequently must be administered in divided doses, whereas chlorpropamide can be given in a single daily dose. Figure 2 compares the half-life values and demonstrates the short half-life of tolbutamide, the intermediary half-life of metahexamide, and the prolonged half-life of chlorpropamide. Another characteristic of chlorpropamide incident to its prolonged half-life is the tendency for blood levels to increase slowly during the first 7 to 10 days that it is used. Figure 3 demonstrates the gradual increase in chlorpropamide blood levels when a constant daily dose is given.[22] The attainment of therapeutic blood levels, however, does not necessarily insure a prompt response. Figure 4 shows that a significant number of individuals respond only after one or two weeks of therapy. If use of the drug is discontinued after only four days, 50 per cent of the patients who ultimately become responsive would be considered resistant to chlorpropamide. This delay in response also suggests that a loading dose should not be used, and that it could increase the danger of hypoglycemia in the responsive patient. Hypoglycemia is an extremely rare consequence of tolbutamide therapy. It might be noted that the urinary degradation products of tolbutamide are insoluble in acid solutions and will produce a flocculation if acid is added to the urine; this may be falsely interpreted as albuminuria.

Due to the current inability to measure accurately the plasma concentration of phenformin, information is lacking in regard to its levels, metabolism and excretion. Because of the rapid manner in which phenformin induces a hypoglycemic response and because it must be administered two to four times during the day, it can be assumed that it is rapidly absorbed and rapidly metabolized or eliminated. Isotopic studies of its excretion in animals point to some degree of elimination by the gastrointestinal tract, but it appears very likely that most of the drug and its metabolites are excreted by the kidney.[23]

When Are They Used?

The extensive clinical utilization of the oral sulfonylurea drugs emphasizes their considerable usefulness. Certain characteristics of the diabetic patient tend to suggest the probability of responsiveness to these compounds. Ideally, patients who are older and have a mild type of diabetes requiring small doses of insulin are most likely to respond. Exceptions to these standards occur frequently and make the determination of absolute criteria illogical. In our experience, sex and weight of the patient and the duration of diabetes have not been greatly helpful in predicting response. A most useful criterion has been the presence or absence of past diabetic ketosis. Patients who become ketonemic with insulin withdrawal almost never respond.

The choice of which sulfonylurea compound to use depends on knowledge of their pharmacology. Tolbutamide, with its shorter half-life and rapid degradation, would appear to have advantages over chlorpropamide in the older patient with mild diabetes in whom the effects of hypoglycemia are feared. On the other hand, chlorpropamide, with its more constant blood levels and slower degradation, would appear to be the choice in patients predictably less likely to respond because of a clinically more severe state of diabetes. In our experience, chlorpropamide has also been effective in a significant number of patients who were regarded as "tolbutamide failures." Table 4 illustrates this advantage of chlorpropamide. While taking an average dose of 1.6 gm. tolbutamide daily, the 10 subjects who comprised group 2 had fasting blood sugar levels ranging from 200 to 380 mg. per cent and were poorly

TABLE 4

RESULTS OF CHLORPROPAMIDE THERAPY IN PATIENTS FORMERLY TREATED WITH TOLBUTAMIDE

PATIENTS	TOLBUTAMIDE THERAPY		CHLORPROPAMIDE THERAPY		
	Mean fasting blood sugar (Mg. per cent)	*Daily dose (Gm.)*	*Mean fasting blood sugar (Mg. per cent)*	*Daily dose (Gm.)*	*P-607* level (Mg. per cent)*
Group 1: Response to both agents (13 patients)	131	1.54	110	0.45	13
Group 2: Response to chlorpropamide only (10 patients)	250	1.60	123	0.57	18
Group 3: Unresponsive (5 patients)	243	1.50	229	0.45	22

*Chlorpropamide.

controlled clinically. After chlorpropamide was substituted in an average daily dose of 0.57 gm. their fasting blood sugar levels fell to an average 123 mg. per cent.[22]

Phenformin may be employed either as a sole hypoglycemic agent or as an adjunct to insulin therapy. In our experience, phenformin has proved effective in some patients who were unresponsive to both sulfonylureas. The same factors of increased severity of diabetes and tendency to ketosis, which make responsiveness to the sulfonylureas unlikely, also apply to phenformin when it is used alone.[24] The use of phenformin as an adjunct to insulin for the purpose of stabilizing the "brittle" diabetic patient has gained considerable popularity.[25] This effect is, of course, difficult to evaluate and may be the result of the intensive care of the patient while initiating therapy with the compound. However, there is no doubt that such stabilization does occur; when it does, it is extremely gratifying. A third possible use of phenformin had been advanced.[26] Phenformin used with a sulfonylurea may induce an additive effect, as each drug has a different mode of action. Such usage might be challenged because of expense to the patient, difficulty in interpreting results, and the possibility of additive toxic effects.

Advantages and Disadvantages

Some of the advantages and disadvantages of these agents are compared in table 5. Tolbutamide has enjoyed the longest and widest use and to date has been reported as having produced the least number of side effects. In addition, it is unlikely that tolbutamide will produce clinical hypoglycemia. By comparison, chlorpropamide is considerably more potent than is tolbutamide, and it can be effective in patients resistant to tolbutamide. However, since it is more potent, it is more likely to produce hypoglycemia, and the incidence of side reactions is higher with chlorpropamide than with tolbutamide. Hypoglycemia induced by large doses of chlorpropamide has been noted especially in elderly patients with organic brain disease. Phenformin offers the advantages of effectiveness in some young diabetic patients and usefulness in stabilization of the brittle diabetic. These advantages are somewhat offset by the rather high incidence of symptomatic gastrointestinal intolerance which attends its use. These effects include nausea, emesis, abdominal cramping and, sometimes, diarrhea; they occur most frequently with higher doses of the drug. A rare patient may complain of unexplainable fatigue and weakness during the time he is taking phenformin.

How Are They Used?

Due to its rapid metabolism, it has been found advantageous to use a loading dose of tolbutamide. Usually 3 gm. is given on the first day, followed by 2 gm. daily until hyper-

TABLE 5

ADVANTAGES AND DISADVANTAGES OF ORALLY ADMINISTERED AGENTS

AGENT	ADVANTAGES	DISADVANTAGES
Tolbutamide	Largest clinical experience to date	Least potent
	Least incidence of side reactions	Often must be given twice daily
	Hypoglycemic reactions very rare	
Chlorpropamide	More potent than tolbutamide	Less total clinical experience
	Effective in many tolbutamide-resistant cases	Hypoglycemic reactions may occur
	Given once daily	
Phenformin	Effective in some growth-onset diabetics	Gastrointestinal intolerance common
	May be useful as adjunct to insulin	

glycemia is controlled. The daily maintenance dose ranges between 1 and 2 gm. In many instances a split dosage of 1 gm. in the morning and 0.5 gm. in the evening is employed because of the short half-life of the drug. Since chlorpropamide blood levels tend to be accumulative during the first week of therapy, we do not advise a loading dose. We usually begin with a dose of 0.25 gm. and either raise or lower it, depending on the response of the patient. The maintenance dose may vary from 0.1 to 0.5 gm. daily, although continued experience has shown that smaller doses are frequently effective. Because of the prolonged half-life of this compound, administration once each morning is sufficient. We do not use the response of the blood sugar to a single dose as a criterion for responsiveness to these compounds because of the previously noted tendency for some patients to show a delayed favorable effect even after two to three weeks of therapy.

Caution must be exercised regarding the size of the initial dosage of phenformin because of the gastrointestinal side effects. These reactions may be minimized if one begins with a small dosage such as 25 mg. twice daily, with breakfast and dinner, and gradually increases the dosage in 25 mg. increments every two to three days. This technic decreases the incidence of gastrointestinal intolerance. Daily doses in excess of 150 mg. are frequently associated with gastrointestinal intolerance. When a satisfactory response to a given dosage occurs without gastrointestinal intolerance, subsequent side effects are quite rare.

Toxicity

In discussing the toxicity or untoward reactions of these drugs, it must be remembered that these compounds are relatively new and that they are used continuously for the treatment of a chronic disorder. Therefore, the incidence of relatively acute manifestations must be supplemented by observations that are obtained over prolonged periods of time. In addition, one would expect a higher incidence of undesirable side reactions during the early phase of development of a new chemical agent, since the optimal dose range, the metabolic activity, and the pharmacologic aspects of the compounds are being assessed.

Table 6 illustrates these factors and quantitates the incidence of reported untoward reactions associated with the use of these drugs. The incidence and type of undesirable side reactions reported to the medical directors of each of the pharmaceutical firms in June 1959 are recorded and compared with the incidence and type of reaction observed at our clinics at the Ohio State University Health Center. As can be noted, the incidence of side reactions obtained in our clinics is higher in each instance. This is due to the fact that in some patients, much higher doses of these compounds were used initially than was subsequently found to be necessary. By the same token, as more physicians recognize the opti-

TABLE 6

PERCENTAGE OF UNDESIRABLE SIDE REACTIONS RECORDED NATIONWIDE AND AT OHIO STATE UNIVERSITY HEALTH CENTER*

SIDE EFFECTS	TOLBUTAMIDE†		CHLORPROPAMIDE‡		PHENFORMIN§	
	Total (9,168 patients)	*OSU (249 patients)*	*Total (5000 patients)*	*OSU (55 patients)*	*Total (2000 patients)*	*OSU (29 patients)*
Hematologic	0.24	0.00	0.60	0.00	0.00	0.00
Dermatologic	1.10	1.20	3.00	0.00	0.00	0.00
Gastrointestinal	1.40	1.20	2.00	3.70	15.00	31.00
Hepatic	0.00	0.00	0.40	1.80	0.00	0.00
Central nervous system	0.00	0.00	0.00	5.60	0.00	0.00
Miscellaneous	0.04	1.60	0.00	0.00	0.00	3.44
TOTAL	2.78	4.00	6.00	11.10	15.00	34.44

*Figures as of June 1959.

Statistics courtesy of: †Dr. C. O'Donovan, Kalamazoo, Michigan, and of ‡Dr. D. Iezzoni and §Dr. H. Sadow, New York.

mal circumstances, dosage and limitations, the untoward reactions will occur far less frequently than recorded in our data. This has been observed by our group specifically in relation to the use of chlorpropamide and phenformin, in which lowering the initial and maintenance doses has resulted in an appreciable reduction in intolerance and toxic reactions. The actual figures are not available at present but we are in the process of accumulating these data; with time, more definite information will be available.

In general, the untoward reactions reported have been sufficiently mild that cessation of therapy or lowering the dosage of the drug has resolved the problem. However, rare instances of severe, irreversible damage involving the hematopoietic, hepatic and dermal systems have been reported; thus, these compounds are by no means completely innocuous. One should also remember that some derangement which is still not apparent possibly may occur with prolonged use, even though this seems less likely with each succeeding year.

In conclusion, the use of any chemically active compound, whether vitamins, acetylsalicylic acid or opiates, is inevitably accompanied by undesirable side reactions. These are minimized by a rigid evaluation of what the physician is trying to accomplish, proper selection of patients in whom they are to be used, understanding of their mode of action and their metabolism, and an awareness of the known hazards accompanying their use.

REFERENCES

1. LOUBATIERES, A.: The hypoglycemic sulfonamides. History and development of the problem from 1942 to 1955. Ann. New York Acad. Sc. 71:4-9, 1957.
2. GOLDNER, M. G.: Historical review of oral substitutes for insulin. Diabetes 6:259, 1957.
3. FRAUK, E., NORTHMAN, M. and WAGNER, A.: Die Synthalinbehandlung des Diabetes Mellitus. Deutsche med. Wchnschr. 52:2017, 2067, 1926.
4. ALLEN, F. M.: Blueberry leaf extract, physiologic and clinical properties in relation to carbohydrate metabolism. J.A.M.A. 89:1577, 1927.
5. LOUBATIERES, A., GOLDSTEIN, L., METROPOLITAUSKI, J. and SCHAAP, J.: Étude expérimentale chez le chien des accidents merveux irreversibles consecutifs a l'hypoglycemie prolongee provaquee par le sulfa-isopropyl-thiodiazol. Comm. 43ème Congrès Medecins Alienistes et Neurologistes de France et des Pays de Langue Française Montpellier. 415 Masson, Ed., Paris, 1942.
6. JANBON, M., CHAPTAL, J., VEDEL, A. and SCHAAP, J.: Accidents hypoglycemeques graves par un sulfamidothiazol (le V. K. 57 ou 2254 RP). Montpellier méd. 21-22:441, 1942.
7. FRANKE, H. and FUCHS, J.: Ein neues antidiabetisches Prinzip; Ergebnisse, klinischer Untersuchungen. Deutsche med. Wchnschr. 80:1449, 1955.
8. KIRTLEY, W. R.: Occurrence of sensitivity and side reactions following carbutamide. Diabetes 6:72, 1957.
9. LOUBATIERES, A.: Action curative du P-aminobenzene-sulfamido-isopropylthiodiazol dans de diabete

sucre humain. Compt. rend. Acad. sc. 241:422, 1955.
10. Goldner, M. (ed.): Symposium: Chlorpropamide and diabetes mellitus. Ann. New York Acad. Sc. 74:407 (March 30) 1959.
11. Ashmone, J. (ed.): Symposium: Insulin and the oral hypoglycemic agents. Metabolism 8:469, 1959.
12. Ungar, G., Freedman, L. and Shapiro, S.: Pharmacological studies of a new oral hypoglycemic drug. Proc. Soc. Exper. Biol. & Med. 95:190, 1957.
13. Pfeiffer, E. F., Pfeiffer, M., Ditschuneit, H. and Chang, S.: Clinical and experimental studies of insulin secretion following tolbutamide and metahexamide administration. Ann. New York Acad. Sc. 82: 479, 1959.
14. Madison, L., Combes, B., Unger, R. and Kaplan, N.: The relationship between the mechanism of action of the sulfonylureas and the secretion of insulin into the portal circulation. Ann. New York Acad. Sc. 74:548, 1959.
15. Williams, R. H. and Steiner, D. F.: Mechanisms of phenethylbiguanide, hypoglycemia. Metabolism 8:548, 1959.
16. Kruger, F., Skillman, T. G., Hamwi, G. J. and Grubbs, R.: The mechanism of action of hypoglycemic guanidine derivatives. Diabetes. (In press.)
17. Pfeiffer, E. F., Steigerwald, H., Sandritter, W., Bänder, A., Mager, A., Becker, U. and Retiene, K.: Vergleichende Untersuchungen von Morphologie und Hormongehalt des Kälberpankreas nach Sulfonylharnstoffen (D 860). Deutsche med. Wchnschr. 82:1568, 1957.
18. Walker, G. and Kinsell, L. W.: Preliminary observations on the effect of intravenous injections of metahexamide on plasma unesterified fatty acid and other lipids in mild diabetes and nondiabetics. Metabolism 8:614, 1959.
19. Williams, R. H., Tyberghein, J. M., Hyde, P. M. and Nielseu, R. L.: Studies related to the hypoglycemic actions of phenethylbiguanide. Metabolism 6:311, 1957.
20. Moorhouse, J. A., Fajans, S. S. and Conn, J. W.: The effects of phenethylbiguanide on pyruvate utilization in man. Clin. Res. 6:405, 1958.
21. Bergen, S. S.: The influence of phenethylbiguanide on ACTH-tolerance tests and NEFA metabolism: Symposium on a new oral hypoglycemic agent, phenformin (DBI). Houston, February 1959.
22. Hamwi, G. J., Skillman, T. G., Kruger, F. A. and Freedy, L. R.: The effects of chlorpropamide on endocrine function in patients with diabetes mellitus and its effect in other endocrine disorders. Ann. New York Acad. Sc. 74:1003, 1959.
23. Wick, A. N. and Stewart, C. J.: Tissue distribution of administered DBI and its relationship to DBI action. Clin. Res. 7:111, 1959.
24. Skillman, T. G., Kruger, F. A. and Hamwi, G. J.: Metabolic and endocrine studies with phenethylbiguanide (DBI). Diabetes 8:274, 1959.
25. Bradley, R. F.: Role of oral blood sugar-lowering agents in the management of diabetes. Ann. New York Acad. Sc. 82:513, 1959.
26. Beaser, S. B.: Therapy of diabetes mellitus with combinations of drugs given orally. New England J. Med. 259:1207, 1958.

Postgraduate Clinical NOTES

141. PURPOSE OF YAWNING

At a British schools' conference some students had an argument about how much (or little) science knows about commonplace things. Here is a question for which they wanted an answer.

QUESTION: What is the purpose of yawning?
ANSWER: The purpose is not, as is commonly imagined, to get more oxygen into the lungs. J. S. Haldane proved that many years ago. It is to expel carbon dioxide, the gas drained from tired blood cells. He showed that, although the body needs oxygen, the mechanism of breathing is governed by carbon dioxide rather than by oxygen. It is the carbon dioxide in the blood which provokes the brain to send messages down to the lung muscles. And a yawn is a convulsive deep breath.

Yawning is highly infectious. That is what makes it social "rudeness"—implying that you are bored. . . . It need not be rude, just imitative, but you will politely smother it as you would smother a sneeze, because it is infectious.

Reprinted from "I weep, therefore I am," by Ritchie Calder,
The UNESCO Courier, March 1960

Rectal Impalement

ERIC F. ROUTLEY*

Long Beach, California

Early diagnosis and treatment are essential in cases of rectal impalement.

Diagnostic procedures include digital examination of the rectum, proctosigmoidoscopy, taking a catheterized specimen of the urine, and roentgenographic examination.

Basic surgical principles must be followed in treatment. Vigorous antibiotic, electrolytic, nutritional and fluid-balance supportive treatment should be employed.

Postoperative treatment includes use of gastric suction until peritoneal irritation has disappeared, maintenance of fluid and electrolyte balance, transfusion of whole blood, and administration of an antibiotic effective against bacteria revealed in the peritoneal culture.

INJURIES of the perineum, anus and rectum are uncommon in civilian practice, but they present a real challenge because of complications and the high mortality rate. In reported cases of rectal impalement, which are rare, mortality rates as high as 80 per cent have been cited, and the injury usually has been associated with such complications as perforation of the rectosigmoid and peritonitis.

ERIC F. ROUTLEY

The term impalement literally means to put to death by fixing on a pale or sharp stake. The term comes from the ancient custom of certain natives who punished their offenders by forcing them to leap onto inverted spears placed in the ground. This usually resulted in death due to peritonitis. At present, the term rectal impalement implies injury of the anus or rectum, associated with intraperitoneal or extraperitoneal rupture, by a foreign body that passes directly or indirectly up the anorectal canal for a variable distance.

*Formerly, Section of Coloproctology, Miami Valley Hospital, Dayton, Ohio; now at Long Beach, California.

Etiology

A review of the literature reveals that rectal impalement has been produced by numerous and bizarre causes including the so-called compressed-air joke, unusual sexual acts, war injuries, sigmoidoscopy, and the improper administration of a barium enema by using a hard rubber nozzle or excessive pressure. In many industrial plants, the workers use a compressed-air nozzle to clean their trousers. As a

practical joke, the nozzle has been placed near the rectum of a fellow worker in order to scare him. In some instances, the sudden release of air has caused perforation of the rectum although the nozzle has not been placed directly against or into the anus.

In one of the reported cases of rectal impalement, a man made a cylinder of firm cartridge paper, inserted it into his rectum, and exploded a firecracker through it. This resulted in a large perforation in the anterior wall of the rectum just below the peritoneal reflection. In another case, a boy who was climbing a tree fell on a stick that was being held by a friend in order to assist him. Impalement also has been caused by falling or sitting on an upright object such as a corn stalk, a pitchfork, the leg of a stool, a piece of wood, the limb or trunk of a tree or bush, a fence picket or post, a cricket wicket, or the post of a bicycle seat. In other cases, children who were sliding down a banister or playground slide have landed on some object that entered their rectum.

Up to 200 years ago in China, lust murderers were executed by rectal or vaginal impalement with stakes or poles. Impalement has been used by some murderers because it leaves little evidence of the crime. King Edward II of England was assassinated by the rectal insertion of a red-hot iron at the instigation of his wife Isabella and her paramour de Mortimer.

Incidence

Rectal impalement is relatively rare in civilian life. It occurs most commonly in young, healthy, active men. It occurs in males three times as often as it does in females.

Disability

The resulting disability is often prolonged and causes serious economic loss. Some authors report that a long period of hospitalization is required in cases of rectal impalement. Seybold, Black and Jackman[1] reported that seven cases of rectal impalement associated with injury of the intraperitoneal viscera were observed at the Mayo Clinic between 1910 and 1939. Death occurred in two of the cases. In one of the other five cases, the patient left the hospital within 30 days. In the four other cases, the patients remained in the hospital for more than 30 days chiefly because of severe infection.

Mortality Rate

In reported cases of rectal impalement associated with peritoneal perforation or involvement of the abdominal viscera, the mortality rates have been as high as 80 per cent. In 179 cases reviewed by Habhegger[2] in 1912, the mortality rate was 26.8 per cent. The mortality rate depends on the age of the patient, the mechanism of injury, the associated shock, the time elapsing between the injury and the institution of the treatment, and on the type of injury, particularly on whether intraperitoneal or extraperitoneal rupture of the anus or rectum has occurred. It must be remembered that the anus and rectum are continuously contaminated by millions of bacteria.

Anatomy

An article by Siler and Bebb[3] contains an excellent review of the anatomy of the perineum, anus, rectum and sigmoid colon. The relationship of the pelvic structures is important in cases in which the patients are females. The perianal space and the extraperitoneal, loose, fatty perirectal tissues may be the site of serious infection in cases of rectal impalement. Other organs such as the vagina, bladder, ureters, uterus and peritoneal cavity are very vulnerable to direct or indirect injury. At operation, it is important to distinguish the intraperitoneal, infraperitoneal and retroperitoneal spaces, and to realize the proximity of genitourinary organs to the rectum.

The configuration of the thigh, buttocks and perineum together with the anorectal canal resembles an inverted funnel. This facilitates the entry of foreign bodies into the anal canal and rectum. A stake may be reflected off the ischial tuberosity and its coverings and may be directed into the anal canal.

Pathology

The impalement may be direct or indirect, that is, the offending object may enter the anal

canal directly or it may pass through the perineum or buttock before it lodges in the anorectal canal. The wound may range from a simple laceration, abrasion or contusion of the anterior wall of the rectum to a contused, jagged, penetrating wound of the rectosigmoid that involves closely related viscera such as the bladder and seminal vesicles in males and the uterus in females.

In cases in which the impalement is direct, the laceration of the rectum commonly is situated on the anterior wall 5 to 8 cm. above the dentate line. The extent of the injury varies with the force of penetration. There may be considerable injury of the soft tissues about the anus, or there may be little evidence of external injury. In cases in which there is a definite history of direct rectal impalement, one must be aware of possible injury of viscera above the rectum. In cases in which the impalement is indirect, a laceration of the perineum or buttock will be obvious. The ischiorectal space may be involved and lead to serious infection. It is easy to overlook involvement of the loose pararectal tissues.

Diagnosis

The history is most important, since it usually will reveal that some object has entered the rectum. Local examination of the perineum, anus and buttocks may reveal only slight bruising or it may disclose extensive injury. The examiner should determine the extent and direction of entry of the offending object. Digital examination of the rectum may reveal only blood on the examining finger, or the examiner actually may be able to palpate a perforation.

If the peritoneal cavity is involved, that is, if perforation has occurred above the peritoneal reflection, abdominal examination at frequent intervals will disclose such signs as tenderness, muscular rigidity, and an absence of bowel sounds. The presence of a laceration usually can be detected by proctosigmoidoscopy. However, this diagnostic procedure may reveal only bruising or a similar lesion. Peritoneal perforation cannot always be diagnosed in this manner because spasm may temporarily close the laceration. A very tiny laceration may cause considerable leaking. No preparation is necessary for this diagnostic procedure, and insufflation of air is not advised.

A catheterized specimen of urine should be examined for blood, and cystoscopy or cystography should be performed if indicated.

Roentgenographic examination—If the injury involves the pararectal tissues, roentgenographic examination may reveal air outside the rectal wall. If peritoneal perforation has occurred, roentgenographic examination with the patient in the erect position will reveal air under the diaphragm. Dilatation of loops of small bowel due to peritonitis may be evident six hours after the injury. Free fluid is present between the loops of bowel in the later stages of peritonitis.

Treatment

The essence of the successful treatment of rectal impalement is to be aware of the possibility of peritonitis and to observe the patient carefully for several hours after the accident. Early diagnosis and treatment are essential. Although antibiotic therapy has been changing so rapidly in the past decade that older forms of treatment have been modified, basic surgical principles still must be followed.

The surgeon must decide whether a perineal, an abdominal or an abdominoperineal operation is required. If the history of impalement is definite, the following procedure has been suggested. Sigmoidoscopy should be performed without anesthesia, without preparation and without insufflation. One should look for evidence of perforation or other injury. A scout film of the abdomen should be made while the patient is in the erect position. One should look for free air under the diaphragm. The patient should be watched carefully for 6 to 12 hours for the development of any abdominal signs. If perforation has occurred, laparotomy should be performed as soon as possible. If operation is performed within six hours after the injury, and if there has not been much spillage of intestinal contents, the perforation should be closed with two layers of interrupted sutures. If there has been much delay prior to doing the operation, and if much spillage or contamination has occurred, a co-

lostomy should be performed proximal to the site of the perforation, and the perirectal spaces and the peritoneal cavity should be drained.

These are sound principles to follow, but exceptions are noted in the literature. Hemorrhage should be controlled, and shock should be treated. Any rupture of the intestine should be closed. Adequate debridement of the wound should be performed, and contaminated extraperitoneal areas should be drained. Transverse or sigmoid colostomy should be performed to protect a weak suture line or to prevent further contamination. The abdomen should be explored whenever indicated, and it also should be explored when a colostomy is performed. If the sphincter mechanism is injured, it should be repaired. Only lifesaving or necessary surgical procedures should be performed if the patient is a poor surgical risk. Vigorous antibiotic, electrolytic, nutritional and fluid-balance supportive treatment should be used.

Conservative treatment should be used for contusions or abrasions about the anus. This treatment includes the use of hot packs, sitz baths and a plastic spray dressing. OXYCEL® gauze-type pads, TRONOTHANE® hydrochloride, cotton balls and KOTEX® are satisfactory for the treatment of more severe injury of the anal and perianal tissues. If the sphincter mechanism has been divided, it should be repaired immediately unless there is evidence that infection is developing. If it is evident that infection is developing, a colostomy should be performed and the sphincter mechanism should be repaired later.

The mesentery should be carefully checked for vascular injuries. A slowly developing hematoma should be treated because it may cause devitalization of a portion of the bowel. A complete tear of the sigmoid mesentery occurred in one of the cases reported in the literature, but resection of the intestine was not necessary. Laceration of the duodenum also occurred in one of the reported cases. The laceration was closed in two layers. An effort should be made to determine whether a foreign body has been retained. Thomas[4] said that tetanus antitoxin and gas gangrene antitoxin should be administered.

The decision regarding the advisability of performing a colostomy depends on the judgment of the individual surgeon. Colostomy is poorly tolerated by children and aged persons. Thomas[4] said that a colostomy should be performed to lessen infection in a case in which there is a large laceration of the rectum that is difficult to close, and in a case in which a severe injury involves the rectum and bladder.

It seems that colostomy is not often required. Placing a substantial rectal tube above the repaired laceration in the rectum may eliminate the necessity for a colostomy. In cases reported in the literature, the time that has elapsed before closure of the colonic stoma has ranged from 32 days to many months. If a colostomy is performed, closure of the stoma should be contemplated in about six weeks. Proctoscopy should be performed about once a week in order to determine the extent of healing of the rectal wound. If diversion of the fecal stream for six weeks has not accomplished the desired result, it is unlikely that diversion for six months will do so. The colonic stoma should be closed intraperitoneally, and a small portion of the colon possibly should be resected. Colostomy may lead to dense adhesions between loops of ileum and colon near the colonic stoma and may cause obstruction of the small intestine.

The following incisions have been used in reported cases in which laparotomy has been performed: (1) a low, left rectus, muscle-splitting incision; (2) a left, lower paramedian, muscle-retracting incision; (3) a low midline incision, and (4) a right, lower paramedian, muscle-retracting incision.

If exploration of the retroperitoneal and perirectal spaces reveals extravasated blood or feces, drainage should be used for 7 to 12 days, and a colostomy should be performed proximal to the site of the injury. Careful debridement is very important, particularly in the ischiorectal space. Perforation of the rectum below the peritoneal reflection may lead to infection not only in the perirectal space but also in the retroperitoneal portion of the abdomen.

The peritoneal cavity should be examined for the presence of blood, fluid and feces.

The surgeon also should attempt to determine whether the bladder, ureters or small intestine has been injured. Kimberly and Koontz[5] reported a case in which the rectum, ileum and bladder were perforated. Colostomy was performed, but the abdomen was not drained. If the urethra is lacerated, it should be sutured with 0000 chromic catgut and should be splinted with a catheter. Suprapubic cystostomy should be performed to divert the flow of urine from the urethra.

The surgeon should examine the duodenum and the entire small intestine from the ligament of Treitz to the ileocecal valve. The patient then should be placed in the Trendelenburg position and the small intestine should be packed off into the upper part of the abdomen. The entire colon should be examined, and the cul-de-sac of Douglas should be checked carefully. One should look for evidence of perforation caudal to the peritoneal reflection, in the root of the mesentery and in the bladder.

If the presence of extraperitoneal blood causes the surgeon to suspect the presence of a retroperitoneal injury, the retroperitoneal area can be exposed by incising the medial and lateral leaflets of the parietal pelvic peritoneum along the edges of the sigmoid colon. The incisions should start distal to the sigmoid branch of the inferior mesenteric artery and should meet anteriorly in front of the rectosigmoid. This procedure will mobilize the colon and will permit upward retraction of the rectosigmoid. It will permit the surgeon to see a perforation of the lower part of the colon or bladder. It also will permit him to close the perforation properly after thorough debridement. This area then should be drained through the lower part of the peritoneal cavity or extraperitoneally.

In cases of extraperitoneal rupture of the anus or rectum, the rupture should be closed if possible, and a loop sigmoid colostomy should be performed. The site of the rupture should be drained adequately by the perineal route. The incisional approach may be perineal, abdominal or both abdominal and perineal. The parasacral perineal approach is preferable to the midline perineal approach used with coccygectomy. If the latter approach is used, there is the risk of infection and prolonged drainage from osteomyelitis which may develop in the lower end of the sacrum.

In cases of intraperitoneal rupture of the colon, the rupture should be closed with silk or catgut. It is possible that wire now is the best suture material for this purpose. If an extensive rupture has occurred in the left side of the colon, as may occur as far proximally as the splenic flexure in cases of air-blast injury, it may be necessary to exteriorize the injured portion of the intestine.

If rupture or injury of the rectum or colon occurs during sigmoidoscopy or during an obstetric procedure, the injured portion of the intestine should be repaired at once with interrupted sutures. As a rule, there is no need to perform a colostomy or to use drainage since there is almost no contamination if the injury is repaired immediately.

Wounds of the soft tissue of the perineum and buttocks should be inspected carefully and should be debrided. They should be left open so that granulation can occur.

Postoperative treatment—Gastric suction should be used until all signs of peritoneal irritation have disappeared. Fluid and electrolyte balance should be maintained, and whole blood should be transfused to replace blood that has been lost. If a peritoneal culture has been made at the time of the operation, one should administer an antibiotic that will be effective against the bacteria revealed by the culture. Neomycin plus a combination of streptomycin and penicillin may be effective; otherwise, streptomycin and penicillin should be administered in massive doses for several days. If gastric suction is not being used and if the patient is able to take medicaments orally, I prefer to administer 250 mg. of TERRAMYCIN® four times a day for four days and 0.5 gm. of neomycin every four hours for 36 hours. This medication plus mechanical cleansing will produce a clean bowel.

Case Report

At about 8 A.M. on February 22, 1957, a seven year old girl jumped out of a house trailer and landed on the leg of an upside-

down stool. The leg of the stool was rammed into her rectum.

The girl was first seen as an outpatient at the hospital about 11 A.M. of the same day. She complained of rectal pain. Bright red blood and clots had been passed from the rectum since the injury, indefinite abdominal pain had occurred, and she had vomited once.

Inspection revealed a ragged laceration on the right side of the anus, involvement of the perianal skin and soft tissues, and a questionable tear of the anal sphincter. Digital and anoscopic examination disclosed fresh and old blood coming from the injured soft tissues and from a site higher in the rectum. The tenderness was too great to permit sigmoidoscopy without anesthesia. The abdominal findings were not significant. It was my impression that the rectum might have been perforated above the peritoneal reflection. The anal and the soft-tissue wounds were cleansed and debrided, and packed with Oxycel gauze. Roentgenographic examination of the abdomen, including roentgenograms that were made while the patient was in the erect position, did not disclose any air under the diaphragm or any other abnormalities.

More definite pain developed in the lower part of the abdomen at about 4 P.M., and vomiting occurred. Examination revealed definite tenderness in both lower quadrants of the abdomen, muscle guarding, and a positive psoas sign. There was no true rigidity. The pulse rate was 140 per minute, and the temperature was 99° F. The leukocyte count was 12,850 per cubic millimeter of blood, and 87 per cent of the leukocytes were polymorphonuclear. A diagnosis of rectal impalement, perforation of the rectosigmoid, and peritonitis was made, and the patient was admitted to the hospital.

She was prepared for operation by means of the usual supportive treatment. Two cubic centimeters of COMBIOTIC® was administered intramuscularly, and 3000 units of tetanus antitoxin was administered. A No. 12 Foley urethral catheter was inserted, and a plastic Levin tube was inserted into the stomach and connected to a Gomco suction apparatus which was operated at a low speed.

Operation was started at 8:35 P.M. and was completed at 10:15 P.M. Anesthesia was produced by the intravenous administration of PENTOTHAL® sodium, and an endotracheal catheter was inserted. The abdomen was opened by means of a lower, left, paramedian, muscle-retracting incision. About 200 cc. of foul, creamy pus was encountered in the lower part of the abdomen and pelvis. Smears and cultures were made with the pus. Careful examination of the small intestine and colon as far distal as the sigmoid did not disclose any abnormality. The rectosigmoid was covered with a fibrinopurulent exudate. At the rectosigmoid juncture, just at the level of the peritoneal reflection, there was a perforation in the anterior wall of the rectum. The perforation was about the diameter of an index finger, and its edges were ragged and necrotic. Spasm of the colon was noted at this site. The peritoneum in the cul-de-sac and over the back of the uterus was torn and badly damaged. The posterior wall of the uterus also was badly torn. The tear was so extensive that a hysterectomy would have been performed if the patient had passed childbearing age.

All necrotic and damaged tissue of the uterus, cul-de-sac and rectum was carefully debrided. Preservation and repair of the uterus resulted in a very thin posterior wall, but it was believed that this would not be a serious handicap since the patient was several years away from the childbearing age.

With some difficulty, the rectal perforation below the cul-de-sac was sutured in two layers with 0 chromic catgut. A large Penrose drain was inserted into the site of the perforation and brought out through the lower end of the abdominal incision. The peritoneum in the pelvis, in the cul-de-sac and back of the uterus was closed around the drain with 00 chromic catgut. A Penrose drain also was placed in the cul-de-sac and brought out through the lower end of the abdominal incision with the drain that was inserted into the site of the rectal perforation. There was no evidence of retroperitoneal contamination extending upward into the posterior part of the abdomen.

The peritoneal cavity was irrigated and aspirated, and one million units of penicillin

and 1 gm. of dihydrostreptomycin were mixed with 10 cc. of physiologic saline solution and instilled into the injured areas.

The colon was full of a rather firm stool, and the advisability of performing a colostomy was considered. However, it was decided that debridement, closure of the wounds, and the insertion of an intraperitoneal and an extraperitoneal drain would be adequate and that a colostomy was not necessary.

The abdominal incision was closed in layers. The peritoneum was closed with a continuous suture of 00 chromic catgut. The rectus fascia was closed by a continuous locking suture of 00 chromic catgut which then was supplemented with interrupted sutures of 00 black silk. A few sutures of 000 plain catgut were placed in the subcutaneous fat. The skin was closed with interrupted sutures of 0000 black silk. Adequate room for satisfactory drainage was left at the lower end of the incision. A safety pin was placed through the end of the extraperitoneal drain, and the intraperitoneal drain was sutured to the skin.

During the operation, 500 mg. of Terramycin was administered intravenously and 0.5 gm. of neomycin was administered intramuscularly. Five hundred cubic centimeters of blood was transfused during and after the operation.

The general condition of the patient was good when she was taken to the recovery room about an hour and a half after the beginning of the operation. She was placed in an oxygen tent for 48 hours. Two cubic centimeters of Combiotic was administered intramuscularly after the operation and twice a day for the next 10 days.

Hematuria occurred on the second day after the operation, but it disappeared in 24 hours without special treatment. Phlebitis of the left leg occurred on the third day, but it responded to the application of hot packs. It apparently was due to exposure of a vein for intravenous therapy.

Examination of the debrided material disclosed evidence of very active inflammation, including many polymorphonuclear leukocytes and lymphocytes, and hemorrhagic infarction.

The bacterial culture that was made at the time of the operation produced gram-negative bacilli that were sensitive to CHLOROMYCETIN®, ACHROMYCIN®, ALBAMYCIN®, and dihydrostreptomycin. The report on the bacterial culture was received on the third day after the operation. Five hundred milligrams of Chloromycetin was administered twice a day by the intravenous route for the next four days. Drainage from the wound was moderate for one week after the operation. A culture of the drainage material was negative on the eighth day. Both of the drains were removed without any ill effect on the tenth day.

Intravenous therapy was used for three and a half days after the operation, and suction through a Levin tube was maintained for the same period. For three days after the operation, 40 mEq. of potassium was administered daily in combination with other medicaments that were being administered intravenously. The administration of DOXINATE® and MILKINOL® was begun on the fourth day. These preparations were administered to soften the stools. SYNKAYVITE® was administered parenterally for six days.

No increase in the temperature or pulse rate occurred after the operation. The leukocyte count was 8500 per cubic millimeter of blood on the third day.

The dermal sutures were removed on the twelfth day after the operation, and the patient was dismissed from the hospital. There was no drainage from the incision at that time. The patient was voiding clear urine, and she was having good bowel movements without any abdominal or anorectal distress. She was up and about and taking a regular diet.

When the patient was observed again on May 20, 1959, two years and three months after the operation, she was perfectly well. She was having normal bowel movements, and she did not have any abdominal or rectal symptoms. Her family physician had seen her several times in the past two years, and he reported that she had been very well on these occasions. It will be interesting to see if normal menstruation and labor occur in later years. It also will be of interest to learn whether any other type of rectal trouble develops in this patient.

Comment

In this case of rectal impalement in a seven year old girl, the rectosigmoid colon and pelvic peritoneum were perforated, and the posterior part of the uterus was sheared off. The diagnosis of peritonitis would have been obvious sooner if the child had been hospitalized for close observation immediately after the injury. Although operation was not performed until about 12 hours after the injury, the result was satisfactory. Needless to say, modern antibiotic therapy and supportive measures helped to produce the successful result.

The fact that colostomy was not performed might be open to criticism. I am very conservative about performing colostomy, especially on young children, and I think that this case is good proof that colostomy is not required in all cases of this type. In many cases in which loop colostomy is performed, it does not divert all of the fecal stream.

REFERENCES

1. Seybold, W. D., Black, R. M. and Jackman, R. J.: Impalement of the rectum. Proc. Staff Meet. Mayo Clin. 19:224 (May 3) 1944.
2. Habhegger, C. K.: Impaling injuries of the pelvis; report of case with review of literature. Wisconsin M. J. 10:449 and 500, 1912.
3. Siler, V. E. and Bebb, K.: Trauma to the perineum, anus, rectum and colon. Am. J. Surg. 80:652 (November 15) 1950.
4. Thomas, L. P.: Impalement of rectum. Lancet 2:704 (October 3) 1953.
5. Kimberly, R. C. and Koontz, A. R.: Impaling injury of rectum: Case report. Am. Surgeon 21:1020 (October) 1955.

Books Received

Books received are acknowledged, and, as space permits, those of principal interest to our readers are reviewed more extensively. Reviews appear in this issue starting on page A-172; additional listings are on pages 755 and A-178.

Law and Medicine. Text and source materials on medicolegal problems. By William J. Curran, LL.M., Professor of Legal Medicine and Director, Law-Medicine Research Institute, Boston University, Boston. 829 pages, illustrated. 1960, Little, Brown & Company, Boston and Toronto. $12.50.

The Physiological Basis of Diuretic Therapy. American Lecture Series. By Robert F. Pitts, M.D., Professor of Physiology and Biophysics, Cornell University Medical College, New York. 332 pages with 38 illustrations. 1959, Charles C Thomas, Springfield, Illinois. $9.75.

Antibiotic Therapy for Staphylococcal Diseases. Antibiotics Monographs. Edited by Henry Welch, Ph.D., Editor-in-Chief, *Antibiotics & Chemotherapy* and *Antibiotic Medicine & Clinical Therapy*, Washington, D.C., and Maxwell Finland, M.D., Associate Professor of Medicine, Harvard Medical School, Boston. No. 12. 208 pages. 1959, Medical Encyclopedia, Inc., New York. $4.50.

Autogenous Vein Grafts and Related Aspects of Peripheral Arterial Disease. By W. Andrew Dale, M.D., Assistant Professor of Clinical Surgery, Vanderbilt University School of Medicine, Nashville. 123 pages with 31 illustrations. 1959, Charles C Thomas, Springfield, Illinois. $6.00.

Gouty Arthritis and Gout; an Ancient Disease With Modern Interest. By Thomas E. Weiss, M.D., Associate Professor of Medicine, and Albert Segaloff, M.D., Associate Professor of Medicine, Tulane University School of Medicine, New Orleans. 221 pages with 56 illustrations. 1959, Charles C Thomas, Springfield, Illinois. $7.50.

Metabolic Care of the Surgical Patient. By Francis D. Moore, M.D., Moseley Professor of Surgery, Harvard Medical School, Boston. 1,011 pages with 143 illustrations. 1959, W. B. Saunders Company, Philadelphia and London. $20.00.

Sexual Impotence in the Male. By Leonard Paul Wershub, M.D., Associate Professor of Urology, New York Medical College, New York. 126 pages with six illustrations. 1959, Charles C Thomas, Springfield, Illinois. $5.75.

The Merck Index of Chemicals and Drugs. Edited by Paul G. Stecher. Ed. 7. 1,641 pages. 1960, Merck & Co., Inc., Rahway, New Jersey. $12.00.

Chemicals, Drugs and Health. American Lecture Series. By John H. Foulger, M.D., Medical Adviser in Toxicology and Forensic Medicine, E. I. du Pont de Nemours and Company, Wilmington, Delaware. 102 pages. 1959, Charles C Thomas, Springfield, Illinois. $4.25.

The Lifespan of Animals. Ciba Foundation Colloquia on Ageing. Edited by G. E. W. Wolstenholme, O.B.E. and Maeve O'Connor, B.A. Vol. 5. 324 pages with 58 illustrations. 1960, Little, Brown & Company, Boston. $9.50.

Plastic Surgical Conditions in Infancy and Childhood

KENNETH PICKRELL, NICHOLAS GEORGIADE, FRANK MORRIS AND JEROME ADAMSON*

Duke University Medical Center, Durham

As a tree grows, it branches. Plastic surgery, like thoracic surgery, neurosurgery, orthopedics, urology and gynecology, is a specialized branch of the general surgical trunk. All surgery, regardless of the sphere, has become more plastic. The meticulous care in handling tissues, the patience, the minute attention to detail, and the ingenuity which plastic surgery demands are being applied in surgical procedures in every part of the body. This budding process has resulted in mutual and intelligent cooperation and coordination of the various specialties to discharge the surgeon's full responsibility to the patient.

Many plastic surgical procedures have been standardized and simplified, and many operations which previously were limited and of value to only a small group may now be carried out effectively by skilled surgeons who are willing to acquaint themselves with the details of the procedures and the management and care of the patient. It is the purpose of this paper to present some of the basic principles of plastic surgery as they apply to some of the more common plastic surgical problems in infancy and childhood. It is intended that the discussion be brief and practical rather than theoretical, and we have not attempted to include all that might be offered by way of alternatives.

A number of operations, if mastered, will produce excellent results in repair of cleft lip. The optimal age is between the first and second months of life.

Correction of cleft palate is highly specialized and technically difficult. A good age for repair is between 14 and 18 months.

Protruding ears can be corrected before the child enters school.

Surgical separation of syndactylous fingers may be postponed until the age of four or five years unless normal growth and development are prevented or the thumb is involved.

A transplant operation using the gracilis muscle has been successful in many cases of rectal incontinence and has also been used to correct urinary incontinence. Five to six years seems to be the best age for the operation.

Congenital Deformities

Deformities resulting from disease or trauma are accepted with consideration and understanding, but the stigma of a congenital deformity may profoundly affect both the child and his parents. Correction of the deformity

*Department of Plastic, Maxillofacial and Oral Surgery, Duke University Medical Center, Durham, North Carolina.

is therefore essential not only to repair the physical defect but also to prevent psychic trauma.

Surgical correction of some of the more common congenital deformities in infancy and childhood depends on the type of deformity, the age and physical condition of the patient, and the degree of the abnormality itself. Some defects are best corrected in early infancy, whereas other defects can and should be corrected later.

Cleft Lip

From the days of Celsus down through the centuries, many writers have described harelip and its repair. This deformity occurs approximately once in every 900 births. It is the result of failure of union of the embryonic parts of the lip, but the cause of this failure is unknown except that there is a hereditary or familial tendency in about 20 per cent of cases. Since fusion of the lip and nose is completed between the sixth and eighth weeks of pregnancy, it is highly speculative that any external cause could be responsible for failure of union or maldevelopment of the lip or palate. The influence of maternal impressions as a cause of congenital deformities must be regarded as a superstition without foundation; the "shock" always occurs long after fetal development has progressed beyond the point where lip or palate union could be influenced. It is probably true that in many instances these statements concerning maternal shock are factual, but that there is a direct relationship to a congenital deformity is impossible.

It has often been said of cleft lip that there is no group of cases in which good results are more important or in which bad results show so plainly. The child's life, future, health, welfare and happiness are at stake when a decision is made to repair the lip. A newborn infant is a poor anesthetic and surgical risk. He has not developed or acquired immunity, his resistance is low, and he is very susceptible to respiratory infection. Anesthesia and operation during the first several days of life may overstrain an already borderline physical reserve. A new baby is not only small, but the structures to be operated on are tiny and fragile.

Optimal time for repair—It is best to repair cleft lip between the first and second months of life. The operation is an elective procedure, and good surgical judgment demands delay until the attending pediatrician or physician advises that the child is in good physical condition for it.

When the continuity of the orbicularis oris muscle is interrupted, the vacuum created by normal sucking is lost. Hence, babies with wide clefts of the lip, alveolus and palate are unable to nurse. If the baby is held and fed in a vertical or upright position instead of being cradled in the arm, and if a nipple with a large perforation or a rubber-tipped Chetwood or Asepto syringe is used, usually the nursing problem is overcome in several days.

Each baby with cleft lip must be managed individually. There are a number of operations which, if mastered, will result in excellent repair of the lip and nose.[1-6] LeMesurier[1,2] revived and revised the original Hagedorn operation, and a high degree of perfection in lip repair is attained with mastery of the principles and execution of this procedure. Steffensen[3,4] also presented a modification of the Hagedorn operation which satisfies all the prerequisites of good repair of the lip and nose: accurate approximation of the muscle, skin covering and mucous membrane linings; a line of repair and suture so designed that its contraction will not cause distortion; a symmetrical mucocutaneous lip line with slight eversion of the lip margin; symmetrical, normal nostril floors; and vertical nostrils with a normal tip (figure 1).

Bilateral cleft lip—Bilateral clefts of the lip are always difficult. Repair of these varied abnormalities defies the selection of a single technic or operation that will insure a good result in any given instance.[6-8] Since the sequelae and stigma of a poor bilateral reconstruction are great, and sometimes lifelong, prudence suggests referral of these cases to a plastic surgeon. The Barsky[7] modification of the bilateral Hagedorn operation has been used with good results. It permits control of the length of the lip and good alignment of the

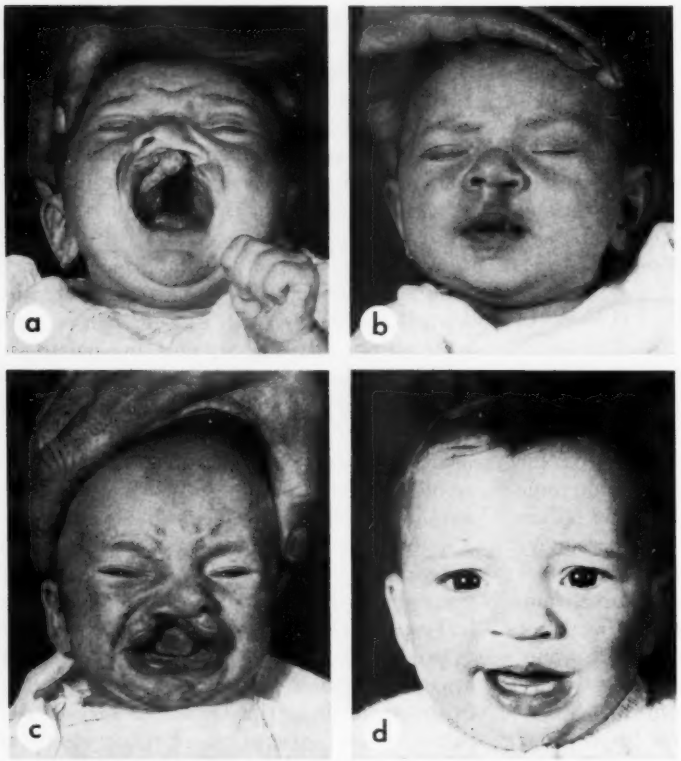


FIGURE 1. Congenital clefts of the lip vary greatly as to the completeness or degree of the cleft, the distortion of the nose, and associated abnormalities of the gum and palate. There is no group of patients in which good operative results are more important or in which poor results show so plainly. The child's life, future, health, welfare and happiness are at stake when reconstruction is undertaken. Hence a high degree of perfection in lip repair must be mastered.

a. Complete cleft of the left side of the lip, alveolus and palate with noticeable distortion of the nose.

b. Appearance of the reconstructed lip one week after operation.

c. Complete cleft of the right side of the lip with associated defects of the nose and palate.

d. Appearance of the lip six months after operation.

vermilion, but at the expense of secondary revision of the columella (figure 2). This secondary revision, however, almost always is necessary regardless of the type of repair employed.

Cleft Palate

Clefts of the palate form another large group of congenital abnormalities which prevent normal function of the mouth, oropharynx and nasopharynx. The aim of reconstruction is to produce a palate which will fulfill the functions of a normal palate: (1) to maintain a mechanical partition between the oral and nasal cavities, preventing the introduction of foreign bodies and food into the nasal cavity with the concomitant possibility of infection; (2) to act as an important adjunct in speech. The volume of air passing through the mouth in speech production is altered by the various positions of the soft palate, the posterior pharyngeal wall, the hard palate and tongue, lips and teeth to produce normal sounds. The nasal chamber merely acts as a resonating chamber. In cleft palate, not only is velopharyngeal closure absent but also, because of the opening in the palate, the volume of air cannot be closed off from the nose and forced through the mouth. Thus the air passes through both the nasal and oral cavities and cannot be altered to produce the proper sounds, and the familiar cleft palate speech results.

A denture may mechanically close off the nasal chamber from the mouth, but a prosthetic appliance cannot produce correct speech. At best an obturator or other appliance is a poor substitute for the patient's own tissues, which, except in unusual instances, can be reconstructed successfully.

The mechanism of nasopharyngeal and velopharyngeal closure, which is extremely impor-

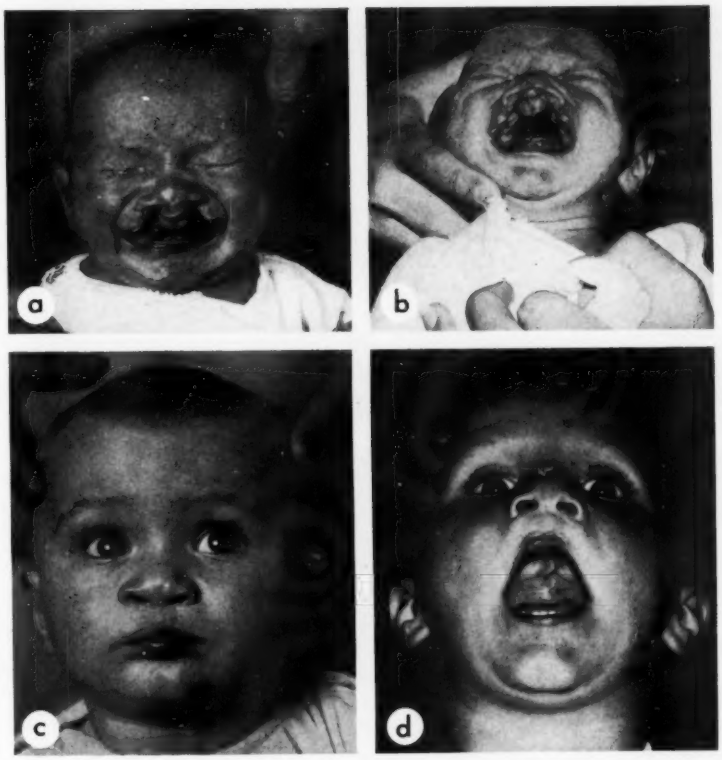


FIGURE 2. The repair and reconstruction of bilateral clefts of the lip defy the selection of a single operation or technic that will insure a good result in a given instance. The sequelae and stigma of a poor bilateral repair are great and are sometimes lifelong. Each baby must be treated individually. A new baby is small, important parts are absent, and those which are present are tiny and fragile.

a and b. Bilateral clefts of the lip, alveoli and palate in a six week old baby.

c. Appearance of the reconstructed lip at nine months.

d. Appearance of the reconstructed palate at 16 months.

tant in correct speech production, may seem rather complicated if it is not understood, but actually is quite simple. The velopharyngeal wall moves forward due to its sphincterlike action, and the soft palate (the velum) moves backward and upward to meet it. The site where the velum strikes the posterior pharyngeal wall is known as Passavant's cushion. The velum itself is raised and moved upward and backward by the levator palati muscles. The tensor palati muscles, when contracting, elevate the velum to the level of the hamular process, but from here on they make the palate tense. Thus, the required velopharyngeal closure so important in speech requires not only a sufficiently long soft palate but also a mobile one.

Of the many operations designed to repair cleft palate, the Wardill[9,10] operation, modified to suit individual variations and requirements, offers a good method of repair (figure 3). However, reconstructive surgical procedures involving the palate are highly specialized and technically difficult. If performed without the benefit of experience and judgment the result may be poor and, even more important, the damage irreparable.

Time of repair—While there is some divergence of opinion regarding the best age for repair of cleft palate, we feel that a good time is between 14 and 18 months of life. The attitude that the malnutrition of an infant with cleft palate is due to the cleft is essentially erroneous. Of course, feeding may be somewhat difficult shortly after birth because of cleft of either the lip or the palate. The remedy is not to subject the undernourished child to the additional strain of operation but first to improve the nutrition by careful feeding. As previously outlined for the infant with cleft lip, feeding should be done with the child in an almost erect position, and he should be fed

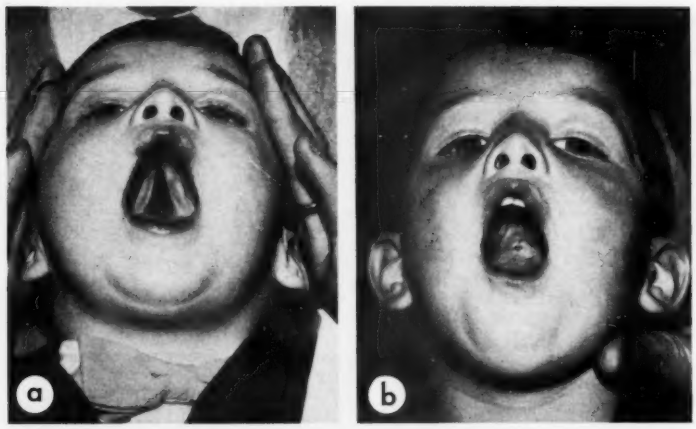


FIGURE 3. Plastic surgery involving the palate, like reconstructive surgery of cleft lip repair, is specialized and technically difficult. If performed without the benefit of experience and judgment, the result may be poor and the damage irreparable. The optimal time to repair a cleft palate is when the child is beginning to talk. This time varies between 14 and 18 months of age.

a. The cleft of the lip was repaired at six weeks of age. The child, now 14 months of age, has just begun to talk.

b. Appearance of reconstructed and lengthened palate at 18 months.

FIGURE 4. Outstanding, protruding or lop ears are a source of embarrassment to children and adolescents as well as to their parents. The jeers and catcalls of playmates may be the basis of severe, concealed psychic trauma. Since the ears are essentially full-grown between the ages of six and seven years, an otoplasty may be performed before the child enters school.

a. A 10 year old boy with outstanding ears of only a moderate degree; yet he was the recipient of unkind remarks by his playmates.

b. Correction required two days' hospitalization. Photograph taken one year later.

very slowly. In a reclining or prone position the child will accept the feeding until the entire nasal chamber is filled with food, and then a violent bout of sneezing and coughing, and possibly aspiration, will ensue. Feedings should be interrupted frequently to allow the nasal chamber to drain. The care of the infant with harelip or cleft palate in the beginning is primarily a pediatric problem, and operation should not be done until he is of the proper age and is in good physical condition.

The speech therapist, the dentist and the orthodontist are important members of the cleft-palate team. The surgeon may build a fine bicycle (the palate), but the patient himself, his parents or a speech therapist must teach him to ride it.

Deformities of the Ears

The many abnormalities and deformities of the ears range from total absence to the common protruding, outstanding or lop ears. These defects are a source of constant embarrassment to the child and his parents. The jeers and catcalls of playmates may be the basis of severe psychic trauma. Correction of protruding ears is not a difficult operation, but considerable experience may be necessary to obtain the desired symmetrical bilateral position and correction (figure 4). Correction of protruding ears depends on the production of a normal anthelix after cartilaginous development is complete. Since the auricular cartilages are fully formed between the ages

FIGURE 5. Syndactylia, a congenital fusion or webbing of the fingers, most often binds the long and ring fingers together, but any pair or all fingers, as shown in a, may be involved. Early surgical separation is indicated when normal growth and development are restrained. When the index finger and thumb are joined, opposition is prevented and functionally the hand is essentially useless.

b. Full-thickness grafts were used to separate the fingers. Individual fingers and hands as units function normally.

of six and seven, a "pin-back" operation[6] can be done before the child enters school.

Total reconstruction of the ear remains the most difficult and least gratifying of all plastic procedures. Restoration of the external auditory canal in complete congenital stenosis is rarely indicated. As a rule these patients have good and useful bone conduction hearing. If the canal is opened, or if one is formed and grafted, without the presence of an eardrum to act as a barrier, infection is invited and chronic otitis is inevitable with resulting loss of the hearing that was present originally. When stenosis of the canal is the result of trauma, the canal can be reopened and lined with flaps of adjacent skin, which do not contract as free grafts do.

Syndactylia

Surgery of the hand demands and demonstrates the dual obligation and responsibility of the surgeon—to restore both function and appearance.

The most common congenital deformity of the hand is syndactylia. Characteristically the congenital webbing or fusion binds the ring and long fingers together, but any pair or all fingers may be involved (figure 5). The webbed fingers act as a single unit, and unless the thumb is involved or there is bony as well as soft-tissue union the joined digits cause little or no functional disability. Early surgical separation is indicated only when normal growth and development are prevented or

when the thumb is involved. When the index finger and thumb are joined, opposition is prevented and functionally the hand is useless. Unless a normal web space for the thumb and index finger is provided during the first year of life, the function, growth and position of the index finger will be distorted by the shorter and eccentrically positioned thumb.

Except in the instances just mentioned, correction of syndactylia may be postponed until the child is four or five years of age. When split-skin grafts are used to reconstruct the web spaces, marked contracture may occur. Therefore one should use either locally rotated flaps or full-thickness grafts. If straight lines of incision are used to separate the fingers, contraction and deformity are inevitable and from a functional standpoint may be worse than the original condition.

Rectal and Urinary Incontinence

The most frequent causes of incontinence in children, exclusive of traumatic lesions, are spina bifida, meningocele, and congenital malformation of the second, third and fourth sacral segments, which supply and control the bladder, rectum and anus. Destruction of the sacral segments or cauda equina results in loss of sensation of the rectum, the bladder, and the saddle area of the perineum. Incontinence may be responsible for almost complete incapacitation, if not from the physical standpoint certainly from the social point of view. Psychologic investigation has shown that incontinent children are social outcasts. While many children can compensate readily for physical or physiologic impairments, no compensation is possible for rectal or urinary incontinence; the child cannot feel, does not know, and cannot tell when he will soil himself. Hence, what little inner security he might be able to build up is soon assailed. Contempt, ridicule and social ostracism are the sequelae.

In 1952 we[11] described the use of the gracilis muscle to construct a voluntary rectal sphincter in children with perineal anesthesia. More than 100 children and adults have been operated on, with uniformly good results and restoration of continence.[12-14] Recently a gracilis muscle transplant operation has been developed to construct a urinary bladder sphincter.[15] Neither the surgeon nor the child and his parents should envision complete automaticity as a result of the operation, but after a short period of training and practice it can be anticipated with reasonable confidence that voluntary function and control can be restored. The gracilis transplant operation, however, should be delayed until the child is old enough to understand what is being done. As each patient must be trained to use the new sphincters, rectal and urinary, he must be able to cooperate and accept the training program intelligently. Five to six years of age seems to be the optimal time for the operation.

REFERENCES

1. LeMesurier, A. B.: A method of cutting and suturing the lip in the treatment of complete unilateral clefts. Plast. & Reconstruct. Surg. 4:1, 1949.
2. ——: The treatment of complete unilateral harelips. Surg. Gynec. & Obst. 95:17, 1952.
3. Steffensen, W. H.: A method of repair of the unilateral cleft lip. Plast. & Reconstruct. Surg. 4:144, 1949.
4. ——: Further experience with the rectangular flap operation for cleft lip repair. Plast. & Reconstruct. Surg. 11:49, 1953.
5. Brown, J. B. and McDowell, F.: Simplified design for repair of single cleft lips. Surg. Gynec. & Obst. 80:12, 1945.
6. Pickrell, K. L.: Plastic, maxillofacial and reconstructive surgery. In Jonas, K. C. (ed.): Babcock's Principles and Practice of Surgery. Philadelphia, Lea & Febiger, 1954, chap. 11.
7. Barsky, A. J.: Principles and Practice of Plastic Surgery. Baltimore, Williams & Wilkins Company, 1950.
8. Brown, J. B. and McDowell, F.: Double clefts of the lip. Surg. Gynec. & Obst. 85:20, 1947.
9. Wardill, W. E. M.: Technique of operation for cleft palate. Brit. J. Surg. 25:117, 1937.
10. ——: Cleft palate. Brit. J. Surg. 16:127, 1928.
11. Pickrell, K. L., Broadbent, T. R., Masters, F. W. and Metzger, J. T.: Construction of a rectal sphincter and restoration of anal continence by transplanting the gracilis muscle. Ann. Surg. 135:853 (June) 1952.
12. Pickrell, K., Masters, F., Georgiade, N. and Horton, C.: Rectal sphincter reconstruction using gracilis muscle transplant. Plast. & Reconstruct. Surg. 13:46 (January) 1954.
13. Pickrell, K. and Georgiade, N.: Correction of rectal incontinence. Am. J. Surg. 90:721 (November) 1955.
14. ——: Gracilis muscle transplant for rectal incontinence. Surgery 40:349 (August) 1956.
15. ——: Gracilis muscle transplant for correction of urinary incontinence. Ann. Surg. 143:764 (June) 1956.

Drugs Most Effective in the Control of Epilepsy

FRANCIS M. FORSTER*

University of Wisconsin Medical School, Madison

The goal of anticonvulsant therapy is threefold: freedom from seizures, freedom from medication, and freedom from the doctor. Good control of seizures can be achieved in 85 to 90 per cent of cases of epilepsy with the armamentarium available at present, but there is a need for new agents with a broader spectrum to help those patients whose seizures are unaffected.

The principal drugs used today are barbiturates, hydantoinates, oxazolidines, succinimides and pyrimidines, but the field of anticonvulsant therapy is expanding rapidly and new preparations are in the investigational stage. There are special indications and contraindications for the various drugs in the various types of seizures.

FRANCIS M. FORSTER

DESCRIPTIONS of epilepsy date back to ancient times, but an effective medication for treatment of the disease was not introduced until 1862, and the manner in which it evolved is rather interesting. Sir Charles Locock, presiding at a meeting at which were presented a whole host of the remedies of the time, commented that he was giving bromides to epileptic patients and they were effective in stopping seizures. His rationale for this treatment was the belief that sexual excesses had something to do with the precipitation of seizures and that bromides decreased sexual desire. This was a rather peculiar neuropharmacologic "long shot" but it did introduce the first effective medication for epilepsy.

The year 1937 might be regarded as the date of the greatest advance in the treatment of epilepsy, in that it brought the "enlightened" period with the introduction of the hydantoinate series of drugs. In the interim between these two dates, surgical treatment began. Of historical interest is the first brain tumor successfully removed in the United States in 1888 by Dr. William W. Keen. I would like to be able to say that Dr. Keen localized this tumor and removed it because of the presence of seizures, but this is not exactly so. The patient, a young man, had convulsions which attracted the attention of a physician, who called for Dr. Keen. There was a large exostosis over a meningioma. Dr. Keen removed the exostosis; the meningioma came along with it! The patient lived for 20 years and was improved.

*Professor and Chairman of the Department of Neurology, University of Wisconsin Medical School, Madison, Wisconsin.

Presented before the forty-fourth annual Assembly of the Interstate Postgraduate Medical Association at Chicago.

Surgical treatment of epilepsy is mandatory in cases of brain tumor and subdural hematoma, and the treatment is directed toward the disease causing the seizures rather than toward the seizures themselves. Surgical therapy also should be considered for patients who have had injuries and who have well-defined scars. The latter patients should be treated first by medical means; if this fails, surgical therapy stands as a second line of defense.

Medical Armamentarium for Treatment of Epilepsy

The drugs employed in anticonvulsant therapy fall chiefly into the following groups: barbiturates, hydantoinates, oxazolidines, succinimides and pyrimidines.

Barbiturates—The leading member of the barbiturate group is phenobarbital, which was introduced in 1912 and is the safest of the anticonvulsant drugs. Its only side effect is drowsiness. Blood dyscrasia has been reported as a complication of its use (as it has even with aspirin), but such an occurrence is so rare that it need not be a serious consideration.

MEBARAL® (methobarbital) is only one-third as effective as phenobarbital. This means that if you have a patient who is taking 0.1 gm. of phenobarbital and you wish to change to Mebaral to avoid the sedative effect, the dose of the latter must be 0.3 gm.

Hydantoinates—DILANTIN® (diphenylhydantoin) and MESANTOIN® (methoin) are the two leading hydantoinates. The minimal effective dose of Dilantin for an adult is 0.3 gm. per day. Giving less than this is wasting the patient's money and the doctor's time. Only about one of every 200 or 300 patients will obtain control of seizures with 0.2 gm. per day, and thus it is wise to consider 0.3 gm. the minimal dosage of Dilantin. The upper dosage limit is 0.6 gm. to avoid toxic signs. Usually, these toxic effects are not serious, generally consisting of ataxia, cerebellar signs and slurring of speech, which disappear quickly when the dosage is reduced. Mesantoin was introduced as a safer and more effective hydantoinate than Dilantin, but it is one of the dangerous drugs, producing aplastic anemia and agranulocytosis. It is one of the drugs one uses when the "going gets tough"—when the other drugs are not controlling the seizures; Mesantoin is in that next line of defense.

Oxazolidines—TRIDIONE® (trimethadione) and PARADIONE® (paramethadione) are the two oxazolidines most widely used, and are interchangeable. The minor complications of their use are rare. One of them is meralopia, which is a fancy way of saying that everything looks brighter than it should. Patients receiving Tridione or Paradione occasionally complain that when they are in sunlight it seems as if they are looking at an overexposed picture or at snow. This effect is transient and disappears quickly when the medication is reduced or stopped. There are also the severe blood dyscrasias which can occur in patients taking oxazolidines.

Acetylureas—All the foregoing drugs are chain compounds. There was one attempt to split the chain. This was the development of PHENURONE® (phenacemide), which has a number of minor side effects and is the most dangerous of all the anticonvulsants because of the anemia and the severe depression it produces. Suicidal depressions have been reported in patients taking this drug. The pharmaceutical house which produces Phenurone is to be congratulated on the way this drug has been dispensed; great care has been taken to make it obvious that this is a dangerous drug.

Pyrimidines—The pyrimidines, represented by MYSOLINE®, are closely related to phenobarbital. Mysoline is one of the most effective of the anticonvulsants and of the newer drugs that we have. The beginning dose is 250 mg. per day. Two complications are seen early in treatment with Mysoline. One is intense nausea and vomiting, which occur in one out of 40 patients. We give the patient a test dose of half a tablet (125 mg.) in the morning, to avoid the occurrence of nausea during the night. The nausea can be counteracted with THORAZINE® and drugs of that type, if necessary. The other complication associated with Mysoline is an intense drowsiness which affects about one out of 10 patients and lasts a week to 10 days. The dosage level does not seem to be correlated with the severity of the drowsiness; the patient seems to be just as

sleepy whether he is taking one, two or three tablets. After about a week, the drowsiness starts to diminish and the patient becomes normally alert again. Therefore, the things to remember in beginning the use of Mysoline are that the patient may have intense nausea and vomiting after a test dose and may have a period of drowsiness of a week or so.

Succinimides—The succinimides (MILONTIN® and, later, CELONTIN®) are safe anticonvulsant drugs.

Other drugs—Bromides are included here for the sake of completeness. In regard to the tranquilizing agents, if any of them have any anticonvulsant effect it is the meprobamate group. The phenothiazines are not effective and, in fact, are apt to be dangerous and to precipitate seizures. Elipten is closely related to DORIDEN® and is a good adjuvant drug which has just been introduced on the market; like Doriden, it may cause acute rash in early stages of treatment. THIANTOIN® (phethenylate) and Hibicon are no longer used.

Identification of the various anticonvulsant drugs—Anticonvulsant drugs often are identifiable by their color and distinctive preparation. Phenobarbital, of course, varies in color depending on who makes it. GEMONIL® (metharbital) is easily identified. Dilantin in the Parke, Davis KAPSEAL® has a red marker around it. Tridione capsules are plain white but taste or smell like coconut when the bottle is first opened; anyone taking a white capsule that tastes like coconut is taking Tridione. Mysoline tablets have AY (Ayerst) on the back. Phenurone tablets are large.

Types of Epileptic Seizures

Epilepsy is not a simple disease, and the results of treatment depend very much on the type of seizures. I shall try to clarify what is meant by different types of seizures. We all know what is meant by a major convulsion—the aura, the cry, the unconsciousness, the tonic and clonic movements, the prolonged unconsciousness afterward. However, sometimes the major seizures are also focal in onset, and this is evidenced by the nature of the aura. If a patient says he has a feeling of impending death which he cannot describe, or that something just seems to come over his head like a cloud before he has a convulsion, this is not a localizing aura. If, on the other hand, he hears music, choral music or symphonies (I have seen such cases), or if he says, "I can draw you the score from the first three bars and then I am unconscious," this patient has a seizure which arises in the temporal lobe, in the area of music appreciation. These are focal seizures, even though they progress to generalized seizures. Likewise the patient who turns his head and eyes to one side probably is having seizures which arise from the frontal lobe, or occasionally from the temporal.

After a seizure, some patients have a period of paralysis of an arm or a leg, or hemianopsia or aphasia. Such focal signs appearing after a seizure indicate a focal onset for the seizure. This does not apply if the patient has had status epilepticus for three or four hours, for then such signs may indicate brain damage due to status epilepticus.

Generalized seizures may be truly generalized or they may be major seizures beginning with a focal aura or a focal onset of deviation, or there may be persistent symptoms later of aphasia and hemiplegia, indicating that they are truly focal.

Petit mal seizures are the short attacks that occur in children. They are uncommon after the age of 20 and extremely rare after the age of 30. The attacks always occur many times in a day. They do not last more than 30 seconds to a minute. They are characterized by blank staring into space and a break in consciousness; occasionally the latter is associated with clonic movements of the arms, head or eyes at a rate of three per second. In this kind of seizure, a generalized three-per-second rhythm is seen on the electroencephalogram. This is the petit mal type of seizure.

Psychomotor seizures are characterized by psychic or motor actions which are purposeful but irrelevant and which the patient does not remember. I know of no better description of a psychomotor seizure than that experienced by a friend of mine, a civics teacher in Philadelphia, some years ago during the war. There was a general assembly, with the

faculty on stage and the student body in the amphitheater. The school band struck up "The Star-Spangled Banner," and everyone stood, faced the colors, and sang—everyone except my friend. He remained seated in the first row, and rubbed the arms of his chair, and during the playing of the national anthem he cursed audibly. Afterward he was unaware of what he had done. This was purposeful action but it certainly was irrelevant. I am happy to say we were able to save his job. He was Jewish, and it wasn't difficult to convince the school board that he was not a Nazi! It was a little hard to becloud what was really going on, but his job was saved. These psychomotor seizures are temporal-lobe seizures, and actually my friend did have a brain tumor from which he subsequently died.

I have talked about major convulsions that have a focal connotation. There are also Jacksonian seizures that start with clonic movements in the thumb and spread to the fingers, up the sides of the face, and so on, to involve one side of the body; and there are other focal seizures, hallucinatory seizures in the course of which patients see images move across their visual field.

Medical Treatment of Various Types of Seizures

With the armamentarium we have at the present time, how can we attack these different kinds of seizures medically? The barbiturates are the best across-the-board medication that we have for epilepsy. They are not as effective as we hoped but they are about the only thing that will work in the various categories of this disease.

The hydantoinates are effective only in major, psychomotor and focal seizures; they are contraindicated in petit mal. The oxazolidines and succinimides are helpful only in petit mal seizures. The pyrimidines (Mysoline) are valuable in major, psychomotor and focal seizures, while Phenurone is used only in the psychomotor group.

In treating patients with major seizures, then, we can draw on the barbiturates, hydantoinates and the pyrimidines (Mysoline). Actually, the choice depends on the severity of the illness and on previous treatment. For simple nocturnal epilepsy, the patient could well be given a dose of phenobarbital at night and a small protecting dose in the morning. An example of simple nocturnal epilepsy would be a college student who on several occasions awakens in the morning feeling groggy and notices a little blood on the pillow, and then one night somebody hears him thrashing around in bed. If the seizures are more severe than this, one could begin with the hydantoinates; Dilantin is the drug of choice, in a dosage of 0.3 gm. per day. As needed, this dosage can be increased or phenobarbital can be added.

If these medicaments are unsuccessful or if the patient has particularly severe disease—seizures every few weeks or several times a week—you may prefer to begin with Mysoline.

In petit mal seizures, phenobarbital has some effect. Perhaps one out of 150 cases will be controlled with phenobarbital alone. When the child is first seen, it is a good working rule to prescribe a small dose of phenobarbital and send him for a blood count and for an electroencephalogram if this is available in the community. When he reports back the next week with the results of these studies, sometimes the mother will say, "He has been wonderful this week, Doctor." When this happens (and it doesn't happen often), it gives you a nice glow because you don't have to go on to Tridione or Paradione or any of the others.

If, as more often is the case, the child is still having spells, you can continue the phenobarbital and add oxazolidine. The phenobarbital protects against the precipitation of major seizures by oxazolidine. In the early days of Tridione we didn't know this. The mother would come back the next week and we would ask, "Has he had any staring spells?" She would say, "No." We would say, "Isn't that wonderful?" And then she would look glum and say, "I don't know, he had a fit and he never had one of those before." This is how we learned to continue the phenobarbital.

If the oxazolidines are ineffective, other agents must be tried, but first the dosage of the oxazolidine is increased to 2.7 gm. per day. It doesn't matter whether Tridione or

Paradione is used first. I prefer Tridione; I think it is a little more effective, and it is also a little more dangerous. We increase the initial dosage of 0.3 gm. every three or four days, adding one tablet at a time until the dosage is nine tablets a day. If the seizures are untouched, we then begin giving eight Tridione tablets and one Paradione tablet every four days. In this way, within two months we know whether or not the oxazolidines are of any help. If they are not, one tries Milontin or Celontin in the succinimide group.

One of the difficult areas in the treatment of epilepsy concerns the children with petit mal seizures who do not respond to any of these drugs. One reaches a point where he feels he is scraping the bottom of the barrel. It is here that the tranquilizers may work; if so, it will be the meprobamate group which are effective. The meprobamates occasionally will control the spells of some of these youngsters. It is here that one tries caffeine, BENZEDRINE®, atropine—almost anything to help these youngsters—and, of course, the new experimental drugs too. Elipten plays its role here, I believe—in the youngsters with petit mal seizures that are not well controlled with any other medication.

In psychomotor epilepsy, the drug of choice is Mysoline. Phenurone is, of course, very effective, but you will recall that this is the one that is so dangerous to blood, bone marrow and liver—and causes psychiatric depressions. There have been suicides among patients taking Phenurone, so one would use it only in a really desperate situation. The drug of choice is Mysoline, and if this is not effective one can add the hydantoinates and phenobarbital. We have had very good results in the treatment of psychomotor epilepsy since the introduction of Mysoline.

Focal epilepsy is best treated with Mysoline as the lead-off drug; Dilantin and phenobarbital are added if necessary.

Comment

With our present armamentarium we are able to bring about good control of seizures in 85 to 90 per cent of the cases. But we are not satisfied. The objective is to stop everyone's seizures. Most of us who work in this field, when we see a patient for the first time, have three goals: to stop the spells, to stop the medicine, and to stop the patient's visits—in other words, complete recovery. These goals are attainable in a large number of cases if the patients will cooperate, and it is necessary to enlist their participation. They must take their medication regularly, and we must not experiment with them. Once the dosage is established it should not be changed. If you know that a patient is seizure-free on 0.4 gm. of Dilantin and 0.1 gm. of phenobarbital per day, he should take these amounts for two or three years. If he has seizures once a month and if three months was the longest interval without seizures before, he should be maintained on this dosage for two, three or four years. You arrive at such a schedule arbitrarily, perhaps, and put a note on the chart and tell the patient, so he has something to aim at. He is in the game with you, now, and he too wants to be seizure-free and should not experiment with his medication. He should know that if he has a seizure after a year or so he will have to start all over. After the arbitrary period of treatment, you can, in many cases, reach the point where the patient is completely free of seizures, free of medicine, and free of the doctor. To do this, the doses of the same medicaments are decreased very carefully—almost as carefully as they were increased in establishing the treatment—over a period of about a year or two.

There is a need for new anticonvulsant drugs. We are never satisfied. For every drug mentioned in this discussion there must be 10 or 15 that go through the hands of those of us who work in the clinics, and 100 that go through the hands of the pharmacologists and the people in the drug houses. Why do we keep on looking? We are concerned about the 10 or 15 per cent of patients whose seizures cannot be completely controlled. We are concerned about the patients who might get a blood dyscrasia because they are taking a relatively toxic drug. We want drugs with a broader spectrum and we want to do a better job of curing these patients. So there is a need to hunt for new drugs.

Pelvic Pain in Women

WILLIAM F. MENGERT*

University of Illinois College of Medicine, Chicago

In the majority of cases, pelvic pain in women has no anatomic basis, yet the desire to eliminate pelvic pain motivates more gynecologic surgery than any other single reason. Only a few of the female genitalia actually have end organs for pain. True causes of pelvic pain arising from the genitalia and other sources are irritation of the peritoneum, traction on a mesentery, distention of a viscus or tissue space, pressure, and spasm or rupture of a viscus.

Physicians cannot always diagnose the cause of pelvic pain, but they can refuse to operate when a pelvic lesion is not found. Only in this way can the common neurotic fixations and chronic pelvic invalidism be prevented.

WILLIAM F. MENGERT

It has been customary to regard all feminine pain located between the navel and the knees as originating in the genitalia, especially if it occurs with or is exacerbated by the menstrual period. Any physician who deals with women is familiar with the patient with chronic pelvic pain. To emphasize that it is an old story, a gynecologist named Mundé in 1879 wrote about the woman who "has a dragging sensation in each groin and down the thighs, some bearing-down and weight in the pelvis, sacralgia, pain in either hip, slight radiating neuralgic pains in the groin or thighs, a numb, sickening pain during coition, and difficult defecation." Even if the genitalia in such a woman are normal, the idea is so ingrained that pelvic pain arises from the genitalia that if we cannot find any disease we invent one. All one has to do is read the transactions of some gynecologic society to realize the many things which have been done over the years for patients with pelvic pain. Today we favor the "cystic" ovary. The day of the retroverted uterus is, fortunately, receding. Chronic pelvic pain is a powerful motivating factor in sending the patient to the doctor. Some years ago Mussey of the Mayo Clinic looked up the records of about 3100 women who came to the Clinic with complaints of pelvic pain, and all we have to remember from that study is that the majority of them had no demonstrable pelvic lesion.

*Professor and Head of the Department of Obstetrics and Gynecology, University of Illinois College of Medicine, Chicago, Illinois.

Presented before the forty-fourth annual Assembly of the Interstate Postgraduate Medical Association at Chicago.

TABLE 1

CLASSIFICATION OF PELVIC PAIN

1. *Pain of intragenital origin* (definite and palpable genital disease)
2. *Pain of extragenital origin* (no genital disease; pelvic organs are anatomically normal)
   a. Pelvic neurosis
   b. Pelvic bone, joint and muscle dysfunction
   c. Diseases of other intrapelvic structures (urinary tract, bowel, etc.)

TABLE 2

INNERVATION OF FEMALE GENITALIA

Somatic (pain directly perceived)—Vulva, vagina, visceral and parietal peritoneum

Autonomic (mediated, referred)—Cervix, uterus, fallopian tube and ovary

I think the desire to eliminate pelvic pain motivates more gynecologic surgery than any other single cause. Many asymptomatic small myomas and cysts on the ovary are removed, and suspensions of the uterus are done, simply because the doctor knows the patient has pain and does not know what is causing it. Once the abdomen is opened at an exploratory operation, it takes more courage than most men possess to refrain from taking out something. For a couple of months after the operation the patient won't have her pain, because the doctor's personality and the events of the operation occupy her mind for this length of time, but if something was taken out and the patient has recurrence of the pain, she can always believe that the doctor didn't take out the right thing or didn't take out enough. By the time a gynecologic consultant sees this patient, she has a battle-scarred abdomen, she has lost her appendix, her uterus has been suspended, and she still has pelvic pain.

Table 1 classifies pelvic pain into two major groups, pain which definitely arises from the genitalia and pain that does not come from the female organs at all. I will use this classification more or less as an outline for the ensuing discussion.

Table 2 indicates how few of the female genitalia actually have end organs for pain. They are the vulva, the vagina and the visceral and parietal peritoneum. You know you can cauterize the cervix in your office without pain to the patient; the uterus has no direct method of producing pain except through the peritoneum over the parts that cover it. The ovary has no means to convey the sensation of pain directly because it is not even covered with peritoneum, so that all of this pain has to be mediated and referred. Table 3 shows the true causes of pelvic pain arising from the genitalia and other sources. These causes are operative throughout the abdomen because, after all, the pelvis is part of the abdominal cavity.

Irritation as a cause of pelvic pain is simple to understand. We can find a lot of causes for irritation. Figure 1 shows our old "friend" pelvic inflammatory disease. This is definitely a source and a cause of pelvic pain. Figure 2 illustrates red degeneration and irritation of a myomatous nodule. Most myomas do not have enough blood supply, and myomas can and frequently do become either degenerated or cystic. A red degeneration like this causes pain, but I think probably the pain is due more to the irritation of the peritoneum overlying the nodule than it is to anything inherent in the myoma. Of course extrusion of the contents of a tumor may also be a cause of irritation. This is not common, but I have seen and operated on patients who had ruptured cystic myoma with fluid in the peritoneal cavity that was highly irritating, and also patients who had ruptured ovarian tumor.

Soon after I went to Dallas in 1943 I encountered a very interesting case. A woman had been drinking beer all Saturday afternoon with a boy friend, and her husband caught up

TABLE 3

CONDITIONS RESPONSIBLE FOR PRODUCTION OF PELVIC PAIN

Irritation of peritoneum
Traction on mesentery
Distention of viscus or tissue space
Pressure
Spasm of viscus
Rupture of viscus

FIGURE 1. Pelvic inflammatory disease.

FIGURE 2. Red degeneration and irritation of a myomatous nodule.

with her about seven o'clock in the evening. Of course, she had a full bladder. He kicked her in the abdomen. That was when I learned the effects of a ruptured bladder and the irritation of the contents in the peritoneal cavity.

Probably the most common source of irritation with which the gynecologist deals is hemorrhage. I was so interested in the effect of hemorrhage in the peritoneal cavity—when, how much, and under what circumstances—that we undertook a study of women who were scheduled for operation and who had relatively normal peritoneal cavities. We took blood from an antecubital vein, and without any alteration of the blood (no citration), using the two syringe method, directly injected blood into the peritoneal cavity. We learned several things. The patients had transient feelings of fullness, pain, aching, tenderness, and even muscle guarding, lasting for minutes to as long as 8 or 10 hours. We learned another interesting thing. One can recall this reaction after it has disappeared by again putting very small amounts of blood into the peritoneal cavity. The inference and the lesson from this are plain. If the sensations I have just mentioned—fullness, aching, pain, tenderness—persist or recur, hemorrhage in the peritoneal cavity either is persisting or has recurred. We did not find much fever or leukocytosis. Usually, we found fever only when the amount of blood injected into the peritoneal cavity ex-

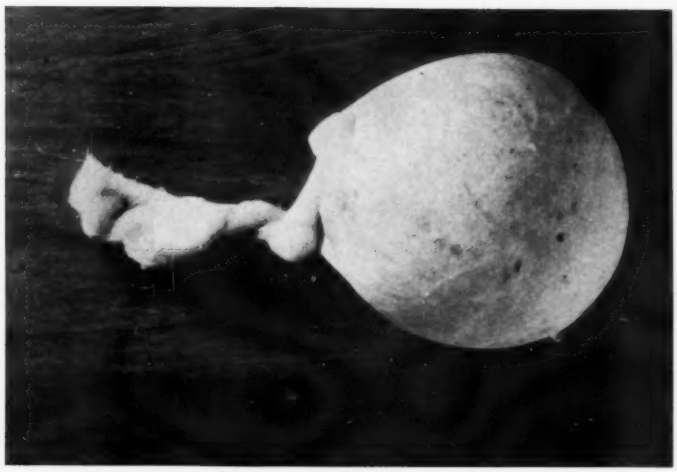


FIGURE 3. Torsion.

FIGURE 4. Endometriosis.

ceeded 400 cc. Occasionally it occurred with a lesser amount, but not often. The elevation of temperature, when it occurred, was seldom more than 1° F. The leukocytosis generally raised the count to a maximum of only about 8000 white cells. We had a few patients during this same time who had massive hemorrhage from other causes, and, of course, this produces shock, which obscures the rest of the picture. I well remember one patient with rather massive hemorrhage in the abdominal cavity. Because she was pretty "shocky" we decided to put her in the Trendelenburg position. When we did so, for the first time she had shoulder pain. So much for irritation as a cause of pelvic pain.

Let us consider the next cause of pelvic pain listed in table 3, traction. We all know that traction on a mesentery causes pain. How can we translate this into obstetric and gyne-

FIGURE 5. An ovarian cyst which distended the abdomen but did not produce pain.

FIGURE 6. A myoma of moderate size without adhesions.

cologic matters? Gynecologically, I think genital prolapse may produce traction, not really on a mesentery but on the supports of the uterus, which in turn produces enough pulling on the parietal peritoneum and on the peritoneum covering the uterine supports to produce a peritoneal type of pain.

Keep these simple facts in mind about torsion, and we will digress a moment. Seldom is there torsion of a big tumor. (See figure 3.) By the time a tumor gets much bigger than a grapefruit I think there is enough friction around the edges, even with the smoothness of the inside of the peritoneum, so that these tumors do not as a rule twist. Generally speaking, it is the small tumor that twists. I am inclined to believe, when there is torsion, that rather than a pulling sensation pain is a matter of interference with blood supply. Probably the nerves accompanying the blood vessels are responsible for the pain.

The next cause of pain arising from the genitalia is rapid distention of a tissue space. Before we translate this to gynecologic matters, let me point out that slow distention of a cyst and slow distention of the urinary bladder do not cause pain. Rapid distention does cause pain, and I think the situation which illustrates this is endometriosis. Figure 4 demonstrates endometrial nodules, which are black. Incidentally, it is impossible today to obtain an illustration like the one in figure 4, because we do not do radical surgery for endometriosis. I think that the endometrial tissue gets under the peritoneum and bleeds at the monthly periods. There is nowhere for the blood to go, it distends the peritoneum, and this causes pain. This brings us to a secondary inference. One little tiny nodule of endometriosis is not going to produce a lot of pelvic pain. The total sum of pain produced by the distention of a peritoneal nodule a couple of millimeters in diameter will not be great. There must be enough nodules, quite a number in fact, before the patient really begins to have pain.

Next as a cause of pelvic pain is pressure. I am extraordinarily skeptical that pressure in obstetric and gynecologic matters ever produces pain. You know that "pelvis" means a funnel, and normally the pelvis is bigger at the top than at the bottom. As an ovarian tumor or a pregnant uterus grows in size to the point where it fills the pelvis, it no longer remains in the pelvis. When it overgrows, it moves up into the abdomen and is no longer an incarcerated tumor. Can a tumor become incarcerated? If the patient happens to have a bony pelvis that is much smaller at the top than at the bottom, the tumor could be incarcerated. Most of the time a tumor is incarcerated because of adhesions, and then I think we must look to the adhesions and to their cause—in

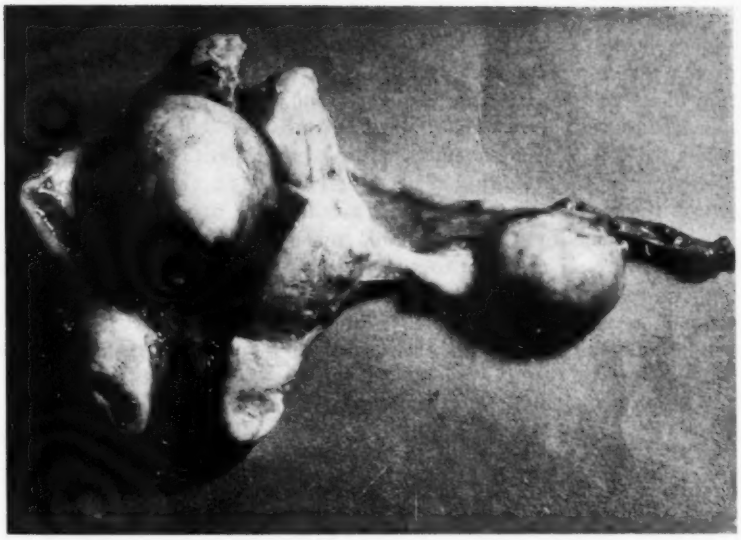


FIGURE 7. A myoma which can produce pain, because it produces spasm.

other words, the underlying disease—for the source of the pain. Figure 5 shows an ovarian cyst removed from a woman who had no pain at all from this tumor which distended her abdomen. The myoma shown in figure 6 had no adhesions and was moderately large.

A myoma of reasonable size will definitely not cause pelvic pain. I remember well operating on a woman of 40 years with a grapefruit-sized, readily movable myoma of the uterus. She complained of pelvic pain. We did a total hysterectomy and conserved her ovaries. She still had pelvic pain. She wanted me to operate again and take out her ovaries, but this time I refused. The type of myoma depicted in figure 7 will cause pelvic pain because it produces spasm of a viscus, in this case the uterus, and represents a foreign body. The uterus tries to expel this foreign body, and pain results from rhythmic uterine contractions. It is a curious thing, but I believe that in this type of situation and also in dysmenorrhea and in labor the uterus represents about the only example of an organ which produces pain in the physiologic exercise of its normal function. From the pathologic standpoint we are all familiar with spasm of a viscus as seen in cystitis and spastic colitis.

The final cause of pelvic pain actually aris-

FIGURE 8. Rupture of uterus.

ing from the genitalia is rupture of a viscus. Figure 8 shows rupture of the uterus. The mark on the top is from a tenaculum. The rupture of an ectopic pregnancy in the fallopian tube also causes pain. I wonder how this causes pelvic pain. When spontaneous rupture of the uterus occurs, or following the use of PITUITRIN®, the woman may say, "I felt a tearing sensation; something tore." I think this can be perceived in a pregnant uterus, which is a big organ, but I question if it is perceived directly as a result of muscle tearing. The patient may be able to feel the peritoneum tear, but certainly not the muscle of the uterus, and in the case of the fallopian tube I do not believe she feels the small peritoneal tear. Then why does she have pain? Probably the introduction of blood into the peritoneal cavity is the basic cause of this pelvic pain.

Pelvic Pain of Extragenital Origin

I believe that the greatest single cause of pelvic pain of extragenital origin is pelvic neurosis. We do not use the term "pelvic neurosis" often enough; in fact we do not talk about it at all. I think it is time we talked about it a great deal. We could cite case history after case history of women who were seen because of chronic pelvic pain on an emotional basis. I remember one with a small myoma, which was thought to be causing her chronic pelvic pain. However, when we talked with the woman and found that she wanted a divorce and learned something about her social situation, we did not operate but encouraged her to get her divorce. She did so, moved elsewhere, and her pelvic pain disappeared. The symptomless small myoma was not the cause of her pelvic pain.

When one considers that the gynecologist deals with one of the two major drives of human existence, namely, sex, one can recognize, I think, that aberrations can easily produce neurosis. I think woman's psyche is much more closely attuned to her genital apparatus than is the male psyche. The first thing that happens to a woman when she thinks that "hubby" has a wandering eye is that she denies him sex. Well, how can she best deny him sex? If she hurts, she is sick. Consciously or unconsciously, this device is used often. Sexual incompatibility, the stress of pregnancy—these contribute to pelvic pain.

Of course, dysfunction of bone, joints, urinary tract and bowel is responsible in a small way for a certain amount of pelvic pain. I should like to contrast the long time it takes to sit down with a woman patient and elicit her story when she doesn't want to give it with the short time required for an ordinary examination or operation. I don't know how long it takes you, but it takes me a good hour at a minimum to dig out the real story from these women and find out what really brought them for consultation. How much easier to operate on her for a small myoma, even if it produces no symptoms.

I have just two more thoughts to express. I believe that in the case of a woman with chronic pelvic pain in which you have exhausted every diagnostic procedure and cannot find anything abnormal, exploration is indicated. I think she should be told ahead of time that there is nothing wrong with her genitalia, but that doctors are fallible and you are going to operate to be sure you have overlooked nothing. If nothing wrong is found, nothing will be removed. Under these circumstances I think exploratory laparotomy is justifiable.

In conclusion, I do not think we can always diagnose the cause of pelvic pain. We can, however, refuse to operate on patients if no true pelvic lesion is found. I think only in this way can we avoid the neurotic fixations and the chronic pelvic invalidism which are so common in women.

The Use of Respiratory Stimulants

JOHN ADRIANI*

Tulane University School of Medicine, New Orleans

Analeptics or antinarcotics may be used to antagonize drug-induced depression of the central nervous system.

Analeptics act primarily on the medullary center and stimulate the central nervous system. They are not effective in reversing an intravenously administered anesthetic or in depressions due to physical agents or an overdosage of a volatile anesthetic or a stimulating drug.

Antinarcotics are weak narcotics rather than stimulants. They exert an antagonistic action only in the presence of an overdosage of a narcotic; they are not effective if the depression is due to excess use of either barbiturates or other non-narcotic hypnotics.

Management of a comatose patient includes establishing an airway, administering oxygen, giving the drug indicated by the type of depression, hydrating the patient, and maintaining the correct fluid-electrolyte balance.

JOHN ADRIANI

In this discussion, I plan to present information which anesthetists have gathered concerning drugs used to antagonize drug-induced depression of the central nervous system. In other words, I plan to discuss the use of stimulants for patients who are comatose from ingesting excessive quantities of hypnotics or narcotics. What do we do for the patient who has ingested an excess of such drugs? Are the available antagonists any good?

When we encounter depression of the central nervous system, as we call this state of diminished reflex activity, we may resort to the use of two types of drugs. We may use analeptics, which stimulate the central nervous system, or antinarcotics. The latter agents are not stimulants, as I shall indicate and emphasize later; they are weak narcotics.

All of us who practice medicine, no matter what our specialty is, instinctively reach for antidotes when confronted with an untoward effect. We tend to think, "What do I have to counteract this?" If we arise with a headache,

*Department of Surgery, Tulane University School of Medicine, and Department of Anesthesiology, Charity Hospital, New Orleans, Louisiana.

Presented before the forty-fourth annual Assembly of the Interstate Postgraduate Medical Association at Chicago.

we take aspirin. We tend toward trying to relieve symptoms, particularly when we are in doubt concerning the factors responsible for the difficulty we wish to overcome.

Two schools of thought prevail concerning the use of respiratory stimulants as antidotes for central depression. One school (I formerly subscribed to this line of thinking) maintains that when dealing with an overdose of a depressant drug the only treatment necessary is to allow the patient to "sleep it off" and to handle it physiologically. The other school believes that stimulants are indicated as adjunctive therapy. I now subscribe to this thinking. I believe that more than supportive treatment is needed and that stimulants are helpful. Stimulants have been with us for many years and will be with us for years to come, no matter what our thoughts are in the matter. Few of us have the necessary patience and the complete confidence in our prognoses to stand optimistically by and allow nature to take its course.

Nature of Drug Antagonism

Stimulants used for overcoming depression of the central nervous system are not true antagonists. They do not neutralize or inactivate the offending drug. In order to make this clear, a brief review of the mechanisms by which physiologic and pharmacologic responses are antagonized is necessary. A particular effect may be reversed by a physiologic antagonist or a pharmacologic opposite. For example, epinephrine antagonizes histamine, and atropine antagonizes physostigmine. Analeptics do not act in this manner.

Another mechanism of antagonism is referred to as competitive inhibition. In competitive inhibition, the response produced by a drug is overcome by another drug which is capable of becoming attached to the receptor to which the first drug ordinarily attaches. The molecule of the competing drug is similar to the physiologically active one as far as the portion which attaches to the receptor is concerned. The structure of the remainder of the molecule is modified sufficiently that the drug is not active physiologically. The receptor portion of the molecule of an antihistamine, for example, is similar to histamine and becomes attached to the receptor to which histamine attaches. The antihistamine, however, is incapable of producing a histamine-like action. Therefore, it antagonizes histamine by denying it access to the receptor site; the antihistamine itself is inactive at this site. Antinarcotics also act by competitive inhibition. The antinarcotic displaces the narcotic from the receptor. The union of the antagonist to the receptor is reversible. Some drugs change the nature of the receptor after uniting with it. Such competition is irreversible and is often referred to as noncompetitive.

Another mechanism of drug antagonism is concerned with enzyme activity. The antagonists act on enzyme systems either to facilitate or to accelerate chemical alteration of a drug. They may act as substrates or as coenzymes and thereby activate new pathways of chemical reactivity in the tissues and cells. Exactly how analeptics exert their effects is not known, but it is possible that they affect coenzyme activity. They do not act by competitive inhibition as far as we know.

Action of Stimulants

Numerous drugs stimulate the central nervous system, but only a few of these are suitable as analeptics because they all do not act in a uniform manner. The drugs used for overcoming depression of the central nervous system act primarily on the medulla. Procaine is a central stimulant, but it is not suitable as an analeptic because it acts on sites other than the medulla. Furthermore, it cannot be controlled. The useful drugs act primarily on the medulla, are controllable, and have a wide safety margin. Caffeine is frequently used as a respiratory stimulant, but it usually is of little or no benefit because its primary site of action is the cortex, not the medulla. Large doses of caffeine, of course, do stimulate the brain stem. Strychnine stimulates the spinal cord primarily. Large doses of strychnine may affect the medullary center but usually not before convulsions appear. Some drugs appear not to have any localized action. For example, atropine seems to act diffusely on the cerebrospinal axis. There is considerable doubt as

to whether or not atropine is a respiratory stimulant.

Drugs act on the medullary center in one of two ways. They may act directly on the central neurons or they may activate the chemoceptors of the carotid body and reflexly stimulate the respiratory system. Lobeline acts on the carotid body. We seldom use it because it has a transitory effect and a cumulative action which leads to undesirable side effects if it is used repeatedly. Lobeline apparently inhibits respiratory enzymes so that the cells in the carotid body react as though the blood oxygen tension were reduced. These drugs, therefore, produce a state which simulates a lack of oxygen in the cells. A number of drugs have a combined effect; they stimulate both the carotid body and the respiratory center. Nikethamide (CORAMINE®) also has a dual effect.

Analeptics

The term "analeptic," which is derived from the Greek, means restorative. Ordinarily, only the brain-stem stimulants are included in this category. The vasopressors, such as epinephrine and ephedrine, are not considered analeptics. Ephedrine has some central action, but it is not of sufficient degree to make it useful as a respiratory stimulant. Vasopressors may be of benefit when the depression is caused by medullary anemia that is the result of hypotension.

METRAZOL® is the best-known conventional analeptic. When administered intravenously, this drug exerts a brief action which lasts two or three minutes. The effect recedes and the dose must then be repeated. Generally, Metrazol is not effective in a heavily depressed patient. The same characteristics are found in nikethamide. Its action is even less startling than is that of Metrazol.

Picrotoxin is a potent, relatively long-lasting drug. Until recently it was the only suitable analeptic available for severe barbiturate-induced coma. We rely on it primarily because it has a relatively long duration of action, lasting a half-hour, three-quarters of an hour, or even a full hour. The peak effect of Metrazol lasts only several minutes. Picrotoxin also has a long latent period. This point should be emphasized because considerable trouble may result if this characteristic of the drug is overlooked. The latent period before the increased reflex activity becomes manifest may be five minutes or more. Sometimes it may take 20 minutes. The temptation to keep injecting the drug is great, but, if one does, serious convulsions may occur. Convulsions due to picrotoxin not only are severe but also last quite some time. I emphasize this because if convulsions develop the situation is serious. The convulsions persist; they are difficult to overcome, and they usually are followed by depression. This depression due to picrotoxin is then superimposed on that caused by the offending drug.

A number of new analeptics have been introduced recently, among which are bemegride (MEGIMIDE®) and methylphenidate (RITALIN®). Both of these drugs have a place in the treatment of barbiturate poisoning, and I have obtained good results with them.

Megimide was first introduced in Australia and it has been studied extensively by British clinicians. It has an advantage over other analeptics in that it not only stimulates the medulla, but it also causes arousal. None of the analeptics used heretofore have exerted this effect. I have never seen picrotoxin effect a reversal from the comatose state to the conscious state.

Ritalin is not quite as effective or as dramatic in producing response as is Megimide. With Ritalin, the reappearance of reflex activity is more gradual and is accompanied by side effects; however, Ritalin is superior to picrotoxin. Arousal does occur with Ritalin, but it is accompanied by nausea, vomiting, disorientation and excitement. In several instances, we have been compelled to sedate patients with a hypnotic other than the offending agent, and I prefer to use Megimide instead of Ritalin.

Both Megimide and Ritalin have a wide margin of safety. Picrotoxin, on the other hand, does not. By this, I mean that the dose which stimulates the medullary center sometimes produces stimulation in other areas of the brain. Twitchings without changes in the

sensorium or increases in reflex activity sometimes occur. When Megimide is used, twitchings do not occur unless one administers the drug rapidly and in excess.

One of the several other new analeptics, DAPTAZOLE®, has not been very impressive. The more recently introduced Vandid, now in the process of clinical evaluation, is allied chemically to Coramine.

The similarities in chemical structure of the analeptics and certain hypnotics are striking. Megimide is chemically allied to the hypnotic glutethimide (DORIDEN®). Bemegride is β-ethyl-β-methyl-glutarimide, while glutethimide is α-ethyl-α-phenylglutarimide. Minor variations in structure of some of the barbiturates convert them to convulsants. Hexobarbital (EPIVAL®) and related N-methyl barbiturates have certain degrees of central excitatory action. Such barbiturates have been known to cause convulsions.

Depressions not affected by analeptics—Analeptics are not effective unless the depression is drug-induced, that is, due to some anesthetic, hypnotic or narcotic drug. For example, a non-narcotized dog receiving picrotoxin, an old stand-by for barbiturate poisoning, shows no response, but suddenly a point is reached at which it begins to convulse. The convulsive dose is administered before medullary stimulation occurs. The same dog given pentobarbital sodium intravenously, followed by picrotoxin, would show signs of respiratory stimulation with a much smaller dose and before the appearance of convulsions. Apparently, these drugs act in the presence of central nervous system depressants. This type of response leads us to suspect that analeptics act on cellular enzymes.

Some respiratory depressions observed are not drug-induced. For instance, a drowned person is apneic because anoxia has inactivated the medulla. Analeptics not only are of no benefit but may even be harmful in such nondrug-induced anoxic states. Likewise, analeptics are not beneficial in respiratory failure due to physical agents, such as cold and electricity. Analeptics are beneficial only in drug-induced depressions.

Respiratory stimulants are unnecessary when a patient is inadvertently overdosed with a volatile anesthetic, such as ether or cyclopropane. In such situations, we merely discard the anesthetic by emptying the breathing bag and administer oxygen by artificial ventilation. This removes the excess concentration in the lung and thereby reduces the blood concentration. Thus, the concentration of the drug in the brain is decreased by first removing it from the blood and the lungs. Of course, it is assumed that the circulatory system is actively perfusing the brain and lungs. Otherwise, neither artificial respiration nor analeptics are of benefit. If the apnea is not reversible, there probably are irreversible changes in the respiratory center, in which case the drugs likewise are of no benefit. We seldom use analeptics when dealing with the volatile anesthetics.

Another situation in which analeptics are not effective is in depression due to the excess use of a stimulating drug. This point requires elaboration. For instance, a rapid intravenous injection of a local anesthetic such as procaine causes a convulsion which is followed by a depression of the central nervous system. A drug which stimulates often depresses if given to excess. Thus, after an accidental overdose of a local anesthetic, an intense depression of the central nervous system develops. The use of stimulants may aggravate the depression; it certainly does not overcome it. We rely on artificial respiration and cardiac stimulants in these situations, but we do not use the central nervous system stimulants.

Certain pharmaceutical firms, of course, are quite enthusiastic about analeptics and advocate their use in the operating room to reverse intravenously administered anesthesia at the conclusion of the operation. The propaganda has considerable appeal to those who are unfamiliar with and have only casual knowledge of anesthetics and their antagonists. The implication is that anesthesia may be completely reversed when one is ready to reverse it. Unfortunately, it is not that simple. It is not as easy as turning the water on and off. Analeptics neither neutralize the depressant drug nor do they hasten its destruction. When used in this manner they cause excitation and dis-

orientation and may even produce convulsions. Their use is indicated only when the patient has areflexia and is severely depressed. Both Megimide and Ritalin are nonspecific stimulants and, when used to excess, may cause convulsions. It originally was thought that Megimide was a true barbiturate antagonist and that it acted by competitive inhibition. This we now know is not the case.

Depressions affected by analeptics—In present-day practice, combinations of drugs are used for anesthesia. Nonvolatile drugs, such as PENTOTHAL® sodium or SURITAL® sodium, are used in combination with volatile drugs, such as nitrous oxide or cyclopropane. Postoperative depressions may occur from these nonvolatile drugs, and analeptics may be of some benefit in such instances.

During the past three years, we have used Megimide or Ritalin to treat more than 125 patients who had ingested barbiturates and other hypnotics. Approximately 70 per cent of these patients were aroused from their coma to the conscious state. The patients who were not aroused showed an elevation of reflex activity. Arousal was noted more frequently when coma was due to the so-called short-acting barbiturates, such as secobarbital sodium (SECONAL® sodium) or pentobarbital sodium (NEMBUTAL®). Failure to cause arousal was noted more often with the long-acting barbiturates such as phenobarbital. Once aroused, the patient remained in an aroused state if depression was due to the short-acting barbiturates. Regression into the comatose state requiring additional analeptics occurred more often with the drugs that are long-acting.

Although our most extensive experience has been with coma due to barbiturates, we also have found both Megimide and Ritalin useful for the depression caused by hypnotics such as chloral hydrate, paraldehyde, glutethimide, NOLUDAR® and meprobamate (MILTOWN®). I have increased the reflex activity of patients overdosed with these drugs, but have not been able to arouse them completely, as we have in cases of overdosage with barbiturates.

Analeptics in light and deep narcosis—There is considerable difference between the response elicited by analeptics in lightly narcotized patients and in those who are heavily depressed. One of our first studies with Megimide was to compare this drug with the conventional drugs. We lightly narcotized patients with 100 mg. Seconal and compared the response to Megimide with that to caffeine, Metrazol, Coramine, Ritalin and Daptazole. In general, there was no remarkable difference in the shortening of narcosis with any of the drugs. The situation was different in heavily depressed patients. In such patients, the conventional stimulants were not nearly as effective as was Megimide.

Reasons for using analeptics—My change in attitude toward the use of analeptics came about after I treated several patients who did not respond to the usual supportive measures without analeptics and whose cardiovascular systems showed progressive deterioration. After the administration of picrotoxin, their general condition improved. We were able to maintain blood pressure within normal limits and adequate ventilation without artificial measures. There is little justification for allowing a patient to remain in a comatose, areflexive state when there is a possibility that reflex activity may be elevated and the sensorium cleared to the point where one may dispense with tracheotomy, artificial respiration and constant attendance by physicians and nurses.

One also must consider another angle—the reactions of the patient's relatives and friends to such a situation. It is difficult to stand nonchalantly by and attempt to assure the family with the retort, "Oh, he is all right; he will soon wake up," particularly when one is not sure that this will be the case. The family is anxious to have something done promptly. It is difficult to assure mamma that little Joey, who has taken three or four of her Seconal capsules, thinking they were candy, will be all right until he is aroused from his coma. Mamma wants Joey awakened as quickly as possible, and there is a good chance that Megimide will do it. We have treated several dozen cases of barbiturate intoxication in children, all of whom had complete arousal.

Objections to using analeptics—There are

several objections to the use of analeptics; some are theoretical and some are practical. The first of these is that analeptics do not help to eliminate the drug. This has been shown repeatedly by the use of radioisotopes. The detoxification and urinary excretion are not influenced. The hypnotic is eliminated no faster with the analeptic than without it. In addition, the body is faced with the task of eliminating two drugs.

Analeptics also may act as depressants. Drugs which stimulate often are biphasic and depress afterward. Such depression occurs if an excess is administered, but it is not likely with subconvulsant doses.

Another objection to the use of analeptics is based on theoretical grounds. We sometimes refer to this as the "armchair anesthetist's objection." The oxygen consumption of a cell is increased when stimulated. This is undesirable in the face of an already existing anoxia. Other objections are that side effects such as nausea and restlessness are undesirable and that convulsions follow if the stimulating dose is exceeded. This happens in lightly narcotized patients in whom the degree of depression was underestimated.

Antinarcotics

The so-called antinarcotics are extremely useful drugs and have much clinical value. At one time or another, we all have had patients who have received an excess of a narcotic for pain relief or premedication. Occasionally, one overestimates or misjudges the dosage of these drugs, and respiratory depression ensues. Errors in computation also occasionally occur. Under these circumstances, we are happy to have either one of two drugs, LORFAN® (levallorphan) and NALLINE® (nalorphine).

Lorfan and Nalline are very similar to each other and to morphine. Nalline is morphine with the methyl group on the nitrogen atom replaced by an allyl group. This change converts morphine from an active, potent narcotic to one which is feeble but which becomes more firmly attached to the cell receptors than does morphine. Therefore, Nalline is capable of displacing morphine from the receptor. Lorfan is levorphanol (DROMORAN®) with its methyl group replaced by an allyl group. Thus, both drugs act as antagonists for narcotics. Both drugs reverse respiratory depression caused by all the drugs derived from opium, such as morphine, codeine, DILAUDID®, metopon, NUMORPHAN®, heroin and dihydrocodeinone, and the new synthetic narcotic drugs such as meperidine (DEMEROL®), anileridine (LERITINE®), methadone, alphaprodine and levorphanol.

Lorfan and Nalline are not suitable for treating overdosage of barbiturates or other non-narcotic hypnotics. If these drugs are administered to patients who have had overdoses of drugs which are not narcotic, they only complicate the situation. These are weak narcotics which displace other narcotics in the cell. They appear to exert their most pronounced effect on the medullary centers. Arousal from the hypnotic state is not so striking a response. These drugs are equally efficacious when given in the proper dosage. Lorfan is three to five times more potent than is Nalline. A dose of 1 to 2 mg. Lorfan usually suffices. The drug does not come under the jurisdiction of the Harrison Narcotic Act, and it is less expensive than Nalline. The latter is made from morphine and, therefore, its sale is governed by the Harrison Narcotic Act. It is treated as a narcotic that causes addiction, and a narcotic stamp and a prescription are necessary for dispensing it, even though it is an antinarcotic.

The antinarcotics are not analeptics. They enhance depression due to non-narcotics, and they produce depression if used in large doses. A subject who has not had a narcotic will be depressed if he is given an antinarcotic alone. Antinarcotics exert their antagonistic action after a narcotic has been used. If administered to an addict, they induce withdrawal symptoms. They do not cause addiction, and they act on the brain stem primarily.

Management of Comatose Patients

The following procedures are recommended in dealing with a patient who is depressed. First of all, an airway must be established. It is very important to support the circulation. Oxygen is started next. Then, one must con-

sider the diagnosis. It is necessary to determine whether a barbiturate, narcotic or some other drug has caused the depression. Sometimes, these drugs depress the vasomotor center in the medulla, and it is necessary to raise the blood pressure with a vasopressor. If the offending drug is a narcotic, usually 5 mg. Nalline is given intravenously. An interval of five minutes should elapse, at which time an additional 5 mg. is given. My experience has been that if the depression is not due to a narcotic, no response develops after administration of 10 mg. I do not give more than 15 mg. Usually, 5 mg. gives some response if the depression is due to a narcotic. If no response is noted, depression probably is due to some other factor.

If an overdosage of a barbiturate is suspected, Megimide in 50 mg. increments is given intravenously. It is advisable to wait three or four minutes between fractions. I have used as much as 750 mg. in patients who have had massive overdosage. The patient seen occasionally who has taken 2 or 3 capsules of secobarbital or other barbiturate wakes up promptly. I have found that Megimide has considerably shortened the hospital stay of such patients. This drug, therefore, does have and will continue to have a very useful place in medicine until a superior drug is found. As I mentioned previously, I am of the school which believes that these drugs are beneficial if they are used judiciously when indicated.

In addition to administration of the appropriate drug, I hydrate the patient, correct any fluid-electrolyte imbalance, and watch closely for relapses. The long-acting barbiturates are more apt to cause relapses. Coma due to glutethimide seems to behave like that caused by the long-acting barbiturates, and it is difficult to reverse.

In view of the theories set forth in this discussion, I believe that respiratory stimulants have a place as adjuncts in treating coma due to overdosage of depressant drugs.

Postgraduate Clinical NOTES

142. MYOCARDIAL INFARCTION

Successful management depends primarily on early and precise diagnosis. The illness can then be more accurately assessed, the probability of complications more readily anticipated, and appropriate therapy begun from the outset. The first problem is the necessity to establish the diagnosis accurately and early.

In assuming responsibility for the management of acute myocardial infarction, the doctor should not hesitate to enlist the diagnostic help which technical procedures can provide. Many conditions masquerade as myocardial infarction. Electrocardiograms and other tests—transaminase levels, sedimentation rates—are not infallible, but in the hands of experienced observers they can provide a standard of accuracy of diagnosis with which the unaided clinician cannot compete. Paton (1957) . . . had a 94 per cent accuracy of electrocardiographic diagnosis as judged by postmortem control. This compared with a 35 per cent accuracy amongst a group of patients in whom death occurred after days or weeks of observation by the physician who elected to place reliance purely on his clinical judgment, without the diagnostic help which electrocardiograms can provide. The moral is obvious.

A. Rae Gilchrist, Problems in management of acute myocardial infarction, *British Medical Journal*, January 23, 1960, pp. 215-219

SYMPOSIUM

Treatment of Multiple Injuries Associated With Automobile Accidents

GEORGE J. CURRY,[1] ERIC OLDBERG,[2]
WILSON WEISEL[3] AND JOHN L. KEELEY[4]

How should an accident victim be transported? What type of head injury precludes immediate treatment of associated injuries? When is tracheostomy indicated? What should be done for a flail chest? If an accident victim has a head injury, a chest injury, abdominal injuries and fractures of the extremities, which should be treated first? These are some of the problems considered. Specific areas of discussion include injuries of the lower extremities, head injuries, crushing injuries of the chest, and abdominal injuries.

Injuries of the Lower Extremities

GEORGE J. CURRY

DR. GEORGE J. CURRY (Moderator): While this meeting is in progress, about 350 people will be killed in traffic accidents in this country and 14,000 will be injured. About 4000 persons are injured every day and 100 are killed. Trauma now ranks fourth as a killer; it occupied third place for quite a while but has been superseded by cancer.

[1]Chief Consultant (Past Chief and Founder), Section for Surgery of Trauma; Chairman, Committee on Graduate Surgical Training, Hurley Hospital, Flint, Michigan.

[2]Professor of Neurology and Neurologic Surgery, University of Illinois College of Medicine, Chicago, Illinois.

[3]Assistant Clinical Professor of Surgery, Marquette University School of Medicine, Milwaukee, Wisconsin.

[4]Professor of Surgery, Stritch School of Medicine of Loyola University, Chicago, Illinois.

Presented before the forty-fourth annual Assembly of the Interstate Postgraduate Medical Association at Chicago.

The immediate treatment of multiple injuries involving the lower extremities demands expeditious application of common sound principles. Webster defines "expeditious" as "characterized by efficiency and rapidity in action"—in other words, it means doing something when it is indicated and doing it quickly. "Expediency" is the responsibility of the person in charge of the injured patient. Good, safe, quick and intelligent transportation is mandatory. Appraisal and evaluation of the

ERIC OLDBERG

WILSON WEISEL

JOHN L. KEELEY

extent of injury without delay are important. The physiologic status of the injured person must be a guide.

Definitive care and immediate care of any injury really begin at the scene of the accident. Subsequent management may be called definitive treatment, but the whole story is really one continuous process. Healing, we know, begins the first minute after injury, and therefore definitive care of the injury in reality starts at the scene of the accident.

Multiple injuries of the lower extremities may involve soft or hard tissue or both. Severance or destruction of main blood vessels may produce loss of life or limb. Damage to other structures is repaired independently or in combination. Obviously, these injuries often are associated with injuries of other parts of the body; that is the theme of this panel, and I like to think that the basic theme may be simply stated as the saving of life and limb.

The patient depicted in figure 1 had complex open fractures of the lower femur with loss of substance and much comminution and bleeding. He also had a craniocerebral injury, a thoracic injury and a questionable abdominal injury. He was transported to the hospital in the proper manner, his injuries were appraised early, and tracheostomy was performed "when we thought of it"—relatively early. The craniocerebral injury was classified as moderately severe. He was taken to the operating room and the bony defect in the femur was explored; this was a matter of necessity and choice because of the extensive bleeding in this area. This brings out the point that in the presence of severe or moderately severe craniocerebral injuries, chest injuries, and sometimes abdominal injuries associated with involvement of the lower extremities of this severity, I think we are justified in trying to take care of the whole situation at one time if the patient's condition permits. I would like to emphasize also the importance of a good team captain. He should be a well-balanced, rationalized and safe general surgeon.

We shortened the leg 2½ in. and removed all the fragments of bone that appeared devitalized, stopped the bleeding, and put in a few immobilizing wires. The x-rays in figure 1b are anteroposterior and lateral views showing the healed femoral fractures nine months later. The leg is 2½ in. short. The patient made an uneventful recovery, has 30 to 40 degrees of motion in the knee, and is employed.

The injury represented by figure 2 requires little description. The obviously extensive damage to the lower extremity in the region of the groin, including the left side of the pelvis, can be seen in figure 2a and b. Excellent transportation to the hospital was available and in my opinion saved this patient's life. The only important intact structure in the injured area was the femoral artery. This injury demanded quick appraisal. There was obvious shock. The decision was made to do a hemipelvectomy (to complete what was started), and I think you will see the reason when you look at the x-ray in figure 2b. An x-ray after hemipelvectomy and the appearance of the patient are shown in figure 2c and d. We told this young man that riding a motorcycle is a dangerous thing for most people to do. On three other occasions subsequent to this injury he was admitted to the hospital because of injuries from riding a motorcycle; once he had a major injury involving his left arm, and the other two times the injuries were of a rather minor nature. I will leave it up to you to figure out how he could ride a motorcycle, but he did; we have, therefore, thought that riding a motorcycle is a disease.

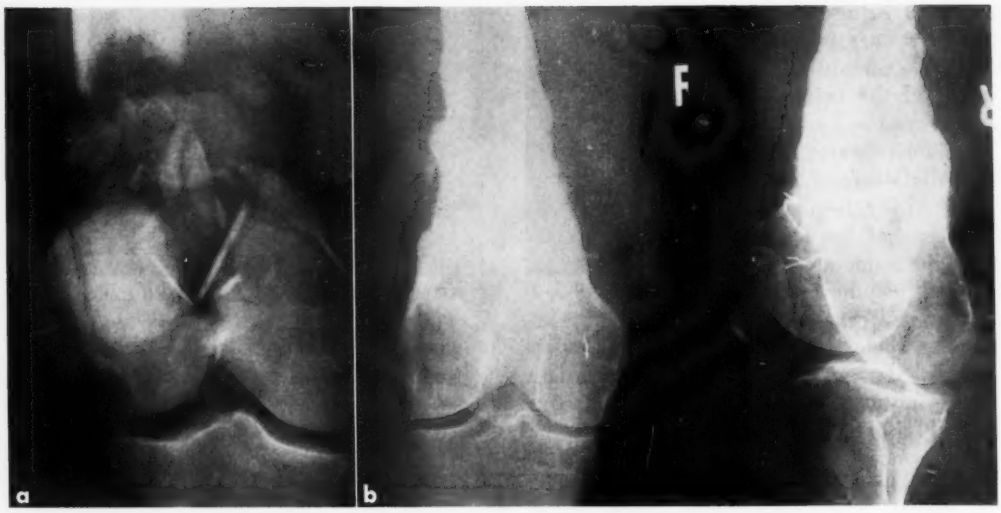


FIGURE 1. a. Anteroposterior film showing complex multiple open fractures of the lower part of the femur with loss of bone and destruction of soft tissue.
b. Anteroposterior and lateral views showing healing of fractures. The injured leg is 2½ in. shorter than the other leg. The patient has 30 to 40 degrees of knee motion and is working.

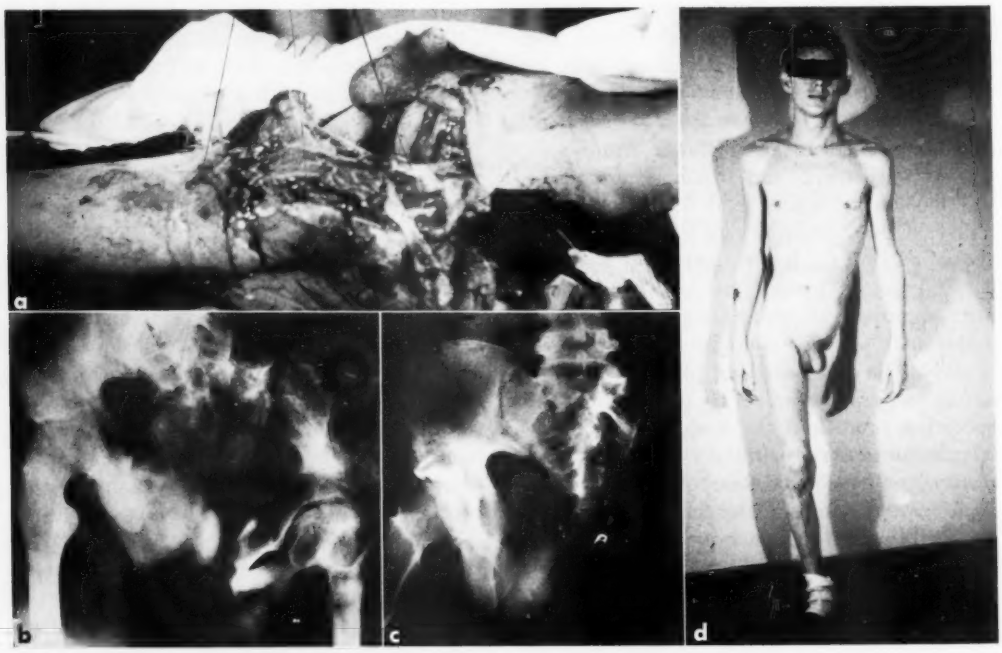


FIGURE 2. a. Multiple injuries to the soft tissue and bone of the left side of the pelvis and groin.
b. Multiple fractures with marked displacement of the left side of the pelvis.
c. Roentgenographic appearance after left hemipelvectomy.
d. Postoperative result.

FIGURE 3. a. Complete lateral dislocation of the right ankle joint without fracture but with disruption of the supporting soft structures and marked circulatory change in the foot.
b. Reduction of dislocation and repair of ankle ligaments.

The injury shown in figure 3a is the only one of its kind I have ever seen. It happened in a traffic accident, and there was complete dislocation of the foot without fractures. All of the soft tissues were damaged, and reduction became a matter of necessity just as quickly as we could do it, because the foot was physiologically inert—practically dead. Figure 3b shows the reduction in plaster, which took about 30 seconds to accomplish; then it took quite a while to repair the neighboring soft-tissue damage to the inner and outer sides of the ankle—the median collateral and lateral collateral ligaments. Again, this case represents expeditious management with no delays —immediately on admission to the hospital.

Figure 4a and b illustrates another example of a severe injury of the ankle in a traffic accident, with no associated soft-tissue damage. Reduction was performed by an intern in the emergency room, without an anesthetic. This decision was proper. The foot was cold, and the intern, realizing that moving the patient to the surgical theater and treating the injury there would mean a delay of 15 or 20 minutes, very properly reduced it without anesthesia. It is a good reduction; there is a slight disparity on the inner side between the medial malleolus and the talus, but at least the foot was saved.

The films in figure 5 represent a similar situation—a "dead foot." Reduction was carried out immediately. I do not advocate reducing these badly injured ankles without anesthesia, but if we are charged with saving a limb it may be necessary.

I hope you will always remember the illustration in figure 6. The attending physician was waiting for the "swelling to go down" before doing something for a badly fractured ankle. The photograph was made five days after the original injury. While the doctor waited for the swelling to go down, the swelling "came up" and he was "bogged down." This result should dispel from anyone's mind the old-time statement, "I'm going to wait for the swelling to go down before doing anything."

Head Injuries

DR. ERIC OLDBERG: The treatment of head injuries has been fairly well stabilized and standardized, but there are many young men out in the field nowadays who sometimes become "eager beavers" and look for things to do. In the treatment of head injuries the watchword is conservativeness within reasonable, sensible limits.

Let us review what one sees every day in the hospital, on the highway, in industry, in

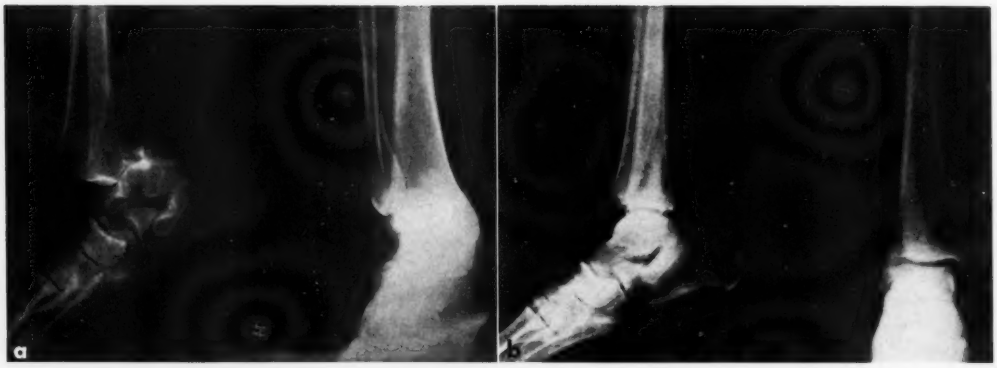


FIGURE 4. a. Posterior dislocation of the foot with associated fracture and circulatory impairment.
b. Result of immediate reduction in the emergency room without anesthesia.

the way of head injuries. As you know, they are among the most common situations in the practice of medicine, no matter what field, and particularly in general practice and general surgery. In fact, they are the most common of all in the practice of the intern or resident in a hospital, because he sees the patients first.

When a patient with a head injury is brought in, there are certain principles to observe which are fundamental. Let us look at a patient who has just been brought to the emergency room. He has been in an automobile accident and is unconscious; he can be aroused slightly, and he may be restless and thrashing around. Perhaps you have to arouse him by pressing on his supraorbital nerve, in which case you get a little response—he begins to move around, makes a face, and tries to push your hand away. Already his face has begun to swell, and maybe one eye has begun to close.

What should one do at this stage? In the situation I have described, the head injury is a closed one; there is no problem of closing a lacerated scalp, nor is there any question of operating on a depressed or a comminuted skull fracture. This is just a matter of a terrific injury to the head; the patient's head is beginning to swell, and he is virtually unconscious but can be aroused slightly. There are certain observations one should make immediately. First one wants to see if the patient moves all extremities—in other words, if paralysis is present. Knowing that it is not, if paralysis develops later you will know it is secondary to edema or hemorrhage or something of that sort but not to an immediate laceration of the brain, which of course would produce immediate paralysis. So, you stimulate the patient just momentarily (it takes me longer to say it than it does to do it). You can press on the supraorbital nerve and see if he moves one hand; do it on the other side and see if he tries to push you away with the other hand. You can jab the soles of his feet with a pin and see if he pulls up his feet. In other words, determine whether or not he moves all of his extremities.

The next thing to do, in what one might call an immediate brief neurologic examination in the examining room, is to look at his pupils. You may not see the pupils in another six hours or so, because both eyes may be swollen shut. It is interesting and important to see if they are equal when the patient is brought in. Whether or not they react, along with all the rest of that business which the interns always write down in the history, is not very important. Do not spend a lot of time stimulating the pupils with light and determining accommodation, and so on. The main thing you want to know is whether or not the pupils are equal. If the patient's injury is a very profound one which may very well cause death within 24 hours or so, he may have unequal pupils when you first see him. If they

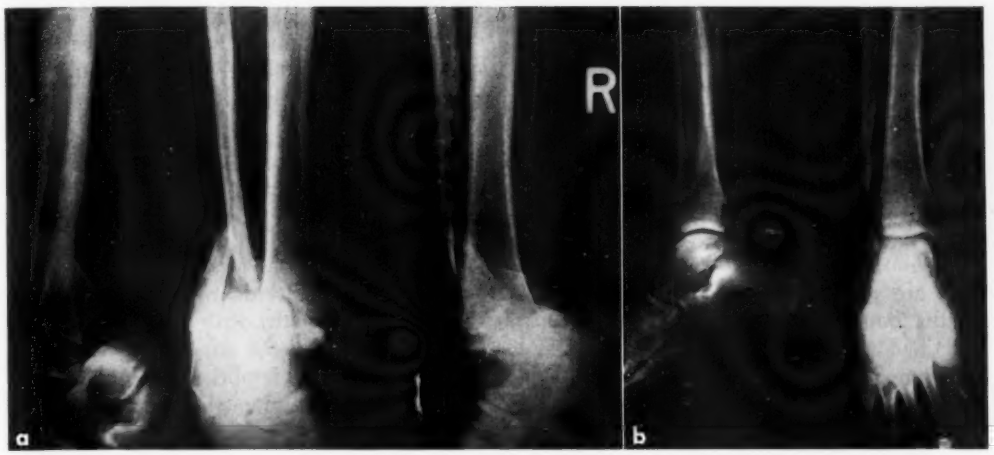


FIGURE 5. a. Multiple fractures of the ankle with posterior and lateral dislocation of the ankle joint and circulatory impairment in the foot. b. Immediate reduction.

are unequal, he has severe injury of the brain and his pupillary reflex connections have been so damaged by contusion or laceration that normal pupillary reflexes are absent. This is a far different situation from the one in which a patient is brought in semiconscious with equal pupils and in the next 12 to 24 hours begins to lapse into unconsciousness and one of the pupils balloons out to two to four times the size of the other one; if that happens, an intracranial hemorrhage is probable, and the usual source is the middle meningeal artery.

If the pupils are equal when the patient is first seen, then you have something on which to base your observations in the next hours and days, because if they become unequal it may be meaningful if taken together with the rest of the findings, such as lapsing into unconsciousness, becoming hemiparetic, etc.

Next, the intern or resident, assuming he is well trained, always whips out his ophthalmoscope and spends about 10 minutes trying to look at the patient's optic fundi. This is utter foolishness, because even if there is four or five times the normal amount of intracranial pressure due to swelling of the brain it takes several days for the optic nerve to swell up sufficiently to be visible with an ophthalmoscope. To waste a lot of time looking in the eyes with an ophthalmoscope for a choked disk immediately after a head injury, or in the first day or two after a head injury, is senseless, unless the patient has had a local injury to the eyeball and you are looking to see if he has a detached retina or something of that sort. Just to look at his optic nerve after a head injury or within a day or two has no meaning; don't waste time doing it. Look at his pupils, and that is all you need to do as far as the eyes are concerned unless you think he might have a detached retina.

The next thing, and I think really the last thing you need to do from the neurologic

FIGURE 6. Multiple fractures of the ankle with marked bleb formation. The attending physician was waiting for the swelling to go down before treating the fractures.

TABLE 1

PRINCIPLES AND TREATMENT OF CHEST INJURIES

1. Maintenance of patent airway
2. Continuation of normal chest mobility
3. Preservation of pleural cohesion
4. Recognition of major intrathoracic catastrophe
5. Prompt treatment of any respiratory distress

standpoint, is to see whether pathologic toe signs are present. The pathologic toe signs are the Babinski sign and all its variations, like Chaddock's, Oppenheim's, Gordon's and Rossolimo's signs—there are a dozen of them, each named after the neurologist who thought his sign was valuable. They all mean the same thing. Babinski's sign consists of upward rather than downward extension of the big toe following stimulation of the sole, and indicates damage to the pyramidal tract. It is an important finding because if present it means there has been considerable embarrassment due to trauma and contusion of the brain itself and, in particular, the pyramidal tracts. The best way to elicit a toe sign is to break a throat stick and stimulate the sole of the foot with half of it.

To sum up the immediate neurologic examination, you determine the patient's state of consciousness (and of all the signs I know of to judge what is happening to a patient, that is the most important), and then you follow his state of consciousness and make an observation about it; you see if he can move all extremities; you see if his pupils are equal; and you test for pathologic toe signs.

When these observations have been made and recorded, the next thing to do is to begin charting the patient's course. You should follow his blood pressure for a time. You follow temperature; you follow respiration, because if he dies he will die from respiratory failure (the ultimate cause of death); and you follow his pulse.

The last point I want to leave with you, and the most important, is this: See that he has a good airway. In days gone by, all sorts of means were used to get a good airway, such as pulling out the tongue with a forceps and holding the chin up. If we cannot get a decent airway with simple methods, we do not hesitate to do a tracheostomy. I have seen a fair number of patients whose lives I am sure were saved because a tracheostomy was done.

Crushing Injuries of the Chest

DR. WILSON WEISEL: As Dr. Curry has intimated, the study of trauma has become a pragmatic pursuit in our modern medical times, dictated by the need to care for increasing numbers of accident victims each year. The apparent apathy with which the general public has viewed the annual appalling attrition of vehicular fatalities appears to have spread somewhat to medical thought. I say this because of the rather constant incidence each year on our surgical services of chest injuries which have received inadequate or improper immediate or definitive care.

Contrary to popular belief, an advance in the treatment of patients does not necessarily mean a progress or progression to something new. In the care of chest injuries this is most apparent, because every year fads are introduced and abandoned. The basic principles which will produce successful solution of these problems were first enunciated in World War I; they were proved, popularized and reaffirmed in World War II; and since that time they have been adequately proved by a tremendous civilian experience.

The principles outlined in table 1, if followed, will give good results in the treatment of chest injuries. I will begin where Dr. Oldberg left off. The need for oxygen for living is obvious, but the frequency with which an open conduit for its delivery to the tissues is overlooked is alarming. If I asked each person in this room to take a deep breath and to hold it as long as he could, few could hold it past one moment. The impact of this need for oxygen and for elimination of carbon dioxide is most apparent in the unconscious patient, where lack of respiration for even one moment may produce irreparable changes in the brain and the heart.

All these principles are directed at one goal, oxygenation of the body. To understand the treatment of injured persons it is necessary to be well acquainted with the fundamental pa-

TABLE 2

PATHOLOGY OF THORACIC TRAUMA

Increased bronchial secretions
Diminished ventilatory and tussive effort
Hemorrhage
Endobronchial
Pleural
Massive (pulmonary-systemic)
Pneumothorax
Peripheral laceration
Central (tracheobronchial rupture)
Open wounds
Mediastinal shifts
Tension pneumothorax
Anoxia, collapse, shock
Diaphragmatic rupture
Left
Spleen, stomach, bowel
Right
Liver
Thoracoabdominal wounds

TABLE 3

PRACTICES IN TREATMENT OF CHEST INJURIES

1. Maintenance of airway, preservation of mobility
Tracheobronchial aspiration
Tracheostomy
Intercostal nerve block
Physical therapy
Assistive respiration
2. Pleural cohesion
Closure of sucking wound
Aspiration of blood
Thoracostomy, removal of air
3. Recognition of catastrophes
Thorough examinations, serial studies
Adequate x-rays
Levin tube (stomach decompression)
Thoracentesis
Endoscopy
4. Emergency thoracotomy

thology that may be encountered. In table 2, which summarizes the pathology of thoracic trauma, I have not emphasized the traumatic lesions of the chest wall. A fractured rib per se is of little significance to the patient. It is the pathologic physiology caused by the injury of the chest wall as well as injury to the underlying viscera that is important to the patient and his welfare.

In an unconscious patient, of course, first attention must be given to the jaw and tongue. In all injured patients, however, airway obstruction usually is iatrogenic, and one sees soon after injury an increase of bronchial secretions and their retention, endobronchial bleeding, and decreased ventilation, setting up a vicious cycle of retained secretions, bleeding, hypoventilation, and suppression of cough. The latter two factors are produced by pain.

These factors are the most immediate threat to the patient's life. All the other items listed in table 2 are, of course, important, but seldom is their immediacy so acute.

The diagnosis of a chest injury is simple. It involves the inspection, palpation and percussion of the chest of a disrobed patient. Whenever a patient is seen who has had a chest injury, one look will give some idea of his color, his chest motions and the degree of respiratory distress. A hand placed on the anterior chest wall can tell you if palpable rales are present. This is a priori evidence of airway obstruction of the type we are discussing. The feel of subcutaneous emphysema and the crepitus of a fractured rib are unforgettable once they are experienced. The location of the apex beat by the palpating finger tells you at once how much the mediastinum may have shifted. Dullness over the chest means blood within the pleural space. A hyperresonant sound means a tension pneumothorax.

This type of diagnosis is all that is necessary in the immediate care of these patients, but this care can be carried out in the emergency room or at the bedside. In taking care of this group of patients (table 3) the most valuable maneuver, in our hands, has been tracheobronchial toilet. Pain is relieved by intercostal nerve block. These two procedures alone will adequately handle the majority of chest injuries. The other practices I have listed in table 3 are reserved for individual patients with conditions that require selective therapy.

The method of tracheobronchial toilet that we utilize is the placement of an endotracheal tube without anesthesia into the trachea, utilizing a Mackintosh blade on a laryngoscope to view the larynx; a small catheter is passed within the endotracheal tube to clear the secretions and bloody material.

An intercostal nerve block is performed, using 1 per cent NOVOCAIN® and injecting 1

TABLE 4

INDICATIONS FOR TRACHEOSTOMY

Secretions not efficiently removed by other methods
Unconscious patient
Injuries of face, head, neck
Emphysematous, elderly and obese patients
Need for continued controlled respiration

TABLE 5

INDICATIONS FOR EMERGENCY THORACOTOMY

1. Hemorrhage
Aortic rupture
Severed intercostal artery
Torn pulmonary artery
Laceration of pleural adhesion
2. Uncontrolled air leak
Tracheal or bronchial injury
3. Rupture of diaphragm
4. Thoracoabdominal wounds or injuries

cc. at each level; in addition to the involved area, we try to inject one or two levels above and below the fractured ribs or the area of pain the patient tells us about. These two maneuvers, as I said before, are sufficient to take care of about 90 per cent of all serious chest injuries which we see. They have to be combined, of course, with reassurance to the patient and with institution of rehabilitative exercises.

Any suspicion of blood within the pleural space should elicit an immediate response of aspiration—and complete aspiration—of the bloody material. Whenever a pneumothorax is present, we prefer to perform thoracostomy under local anesthesia and insert an intrapleural catheter for decompression with subaqueous systems.

In any discussion of serious or crushing injuries of the chest, one must mention paradoxical respiration. This term simply refers to the contrary movement of the chest wall. During inspiration the chest wall moves inward; during expiration it moves outward. This is usually due to fractured ribs or fractured sternum. In our experience, however, it is always due to airway obstruction with or without these other items. The most significant thing about this type of pathologic physiology is the fact that when *pendeluft* (a term designated by a German physiologist) occurs, hypoxic air transfers from the bad lung to the good lung, setting up a vicious cycle leading to anoxia, and eventually, with the mediastinal shift, there appear unwelcome cardiovascular changes and responses. A similar physiologic situation is seen in open chest wounds. Fortunately these are rare in civilian practice, and their immediate treatment is simply to cover the opening which is hissing and making a sound with loose VASELINE® gauze.

Indications for tracheostomy and for emergency thoracotomy, and some "do's and don'ts" in chest trauma are given in tables 4 to 7. If these practices are followed and if treatment is instituted sufficiently early, there should rarely be a fatal chest injury.

Abdominal Injuries

DR. JOHN L. KEELEY: Abdominal injuries may occur in combination with injuries to any other region, and they pose difficult problems in diagnosis and in deciding for or against surgical exploration. Do the signs and symptoms justify exploratory laparotomy? We are concerned here with the patient who has multiple injuries. Most of these result from traffic accidents. The wide range of incidence of multiple injuries (from 10 to 60 per cent) may be due largely to statistical variations. There may be combinations of injuries involving the extremities without any damage to the head, chest or abdomen. In some patients there are head injuries plus other damage, and in others, damage to the trunk plus injuries to the urinary tract. The damage which threatens life may dictate which consultant is the most urgently needed. Usually the general surgeon is the one who is the team captain; he should guide the whole program and evaluate the advice of his consultants.

The sequence of treatment is important, and I thoroughly enjoyed Dr. Oldberg's presentation of what he would like to know about the patient with a head injury. Certainly there are not very many patients whose lives are going to be endangered immediately because of a head injury. First of all, as Dr. Weisel pointed out, we must have a living patient. Once we

TABLE 6

DO'S IN CHEST TRAUMA

Examine patient carefully
Secure adequate x-ray studies
Aspirate tracheobronchial tree
Close sucking wounds
Keep pleural space dry
Insure efficient ventilation
Emergency surgery for catastrophes

TABLE 7

DON'TS IN CHEST TRAUMA

Overlook or neglect chest injuries
Give opiates
Strap chest
Give oral feedings early
Forget x-rays
Restrain patient unnecessarily
Allow retention of bronchial secretions

have made sure he has an adequate airway, and good respiratory function, we must look for signs of injuries to the abdominal viscera. Many patients with multiple injuries die from peritonitis or intraabdominal hemorrhage from an injury to an abdominal structure that was overlooked.

The repair of open injuries to bone and muscle certainly would not take priority over abdominal injuries. Definitive care of closed fractures and lacerations is undertaken only when the patient is responding to adequate care for his more serious and life-threatening injuries.

As Dr. Curry well understands and emphasizes in his teachings, it is certainly worthwhile to treat all of the patient's injuries as soon as possible so that hospitalization will not be prolonged because of delay in such matters as reducing a fracture or repairing lacerations during the period when resuscitation of the patient is progressing satisfactorily.

Figure 7 shows a patient with multiple injuries. Fortunately, she did not have abdominal injuries. However, she did have fractures of an arm and a leg, she had a head injury and was unconscious in the early part of her hospitalization, and in addition she had a "stove-in" chest—the paradoxical motion Dr. Weisel described. Pneumothorax was treated by a thoracostomy tube. A tracheostomy permitted effective and frequent aspiration of secretions and the assistance of respiration by mechanical means. Traction applied to pectoral musculature stabilized the chest wall. Our problem was to determine whether or not there was an abdominal injury that should be investigated surgically.

The most important basis for making this decision was information obtained by repeated observations. A graphic chart for recording blood pressure, pulse, respiratory rate and temperature was immediately begun. Another great aid in a complicated situation involving multiple injuries is a protocol which records chronologically all observations, findings, treatment, etc., so that one has a picture of the changing scene. Trends which indicate that conservative treatment is no longer justified are detected as early as possible from these accurate observations.

The importance of a graphic chart and a protocol as described cannot be emphasized too strongly. One knows very little about the injured patient prior to the first examination and therefore a base line must be established. Treatment must be determined by the general trend of his course after he is brought to the hospital. In addition to the chart and protocol, I believe that re-examination at frequent intervals ought to be made by the same observers if at all possible. We have kept residents up all night (this applies to attending staff too) making observations at hourly intervals so that there would be continuity of clinical opinion. Thus, increasing distention, tenderness or dullness and decreasing peristalsis which suggest progression of intraabdominal damage will be appreciated without delay.

In the immediate management of the patient with multiple injuries, one should begin by suspecting the worst. Once respiratory problems and serious head injury have been ruled out or evaluated and treated, appropriate measures for treatment of shock is the most urgent consideration. The need to control external bleeding is, of course, obvious, and the extent of blood loss thus incurred may be sug-

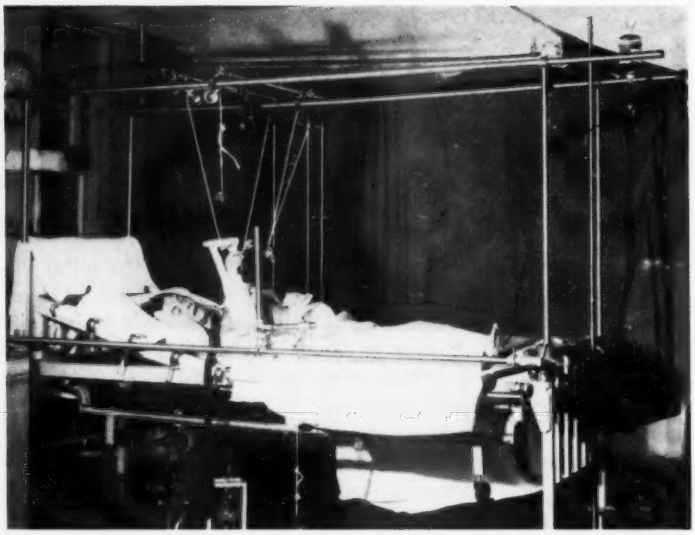


FIGURE 7. Photograph of patient who sustained multiple injuries in a traffic accident. A head injury caused unconsciousness. Fractures of an arm and a leg were treated by traction. The "stove-in" chest was treated by thoracostomy tube for pneumothorax, and tracheostomy permitted frequent aspiration of secretions and assisted respirations by mechanical means. No abdominal problem requiring laparotomy developed.

gested by clinical examination, by visible evidence of loss at the site of injury, in clothing, dressings, etc., and by response to transfusion.

Concealed hemorrhage must not be overlooked. Serial hematocrit and hemoglobin estimations are the best guides to therapy. Hemorrhage at fracture sites may be extensive. It is estimated that in the presence of a fractured femur an increase of 2 in. in the girth of the thigh indicates the loss of 1500 to 2000 cc. of blood into the soft tissues of the area. In a patient seen recently who had multiple pelvic fractures, 1500 cc. of blood was required to restore measurable blood pressure, and this without any loss of blood except at the fracture sites.

In the presence of abdominal trauma plus evidence of hemorrhage, one must consider bleeding from a ruptured spleen, torn mesentery, "fractured" liver or kidney, or any part of the gastrointestinal tract.

The insertion of a catheter to measure urinary output and to detect bleeding into the urinary tract or from bladder injuries should be done early. A Levin tube to determine gastric bleeding is likewise in order.

Relief of pain merits comment. A patient in shock who receives morphine or DEMEROL® subcutaneously may have so little circulation that he does not get much effect from the drug. This may lead to a second dose; and later, when his circulation has improved, the drug may cause serious depression at a time when its administration has been forgotten. It is much better to use these pain-relieving agents intravenously so that the effect can be assessed promptly. They should be given slowly in small doses and, if necessary, repeated at intervals.

The regional findings in abdominal trauma deserve careful attention. Some external evidence, such as abrasions or ecchymoses, is seen in about 50 per cent of the patients. Nonpenetrating forces may damage the solid organs such as the liver, spleen and kidneys and the gastrointestinal tract, particularly at points of fixation, for example, at the beginning and the end of the small bowel and at the hepatic and splenic flexures of the colon. *In any patient who has sustained direct or indirect abdominal trauma, suspect the worst.*

In many patients who have sustained trauma not only to the abdomen but also to the chest or back, abdominal distention and tenderness develop, with decreasing or absent peristaltic sounds. Some of these signs are reflex in nature and do not mean that morphologic damage has occurred to intraabdomi-

TABLE 8

VULNERABILITY OF ABDOMINAL VISCERA; ORDER OF FREQUENCY OF DAMAGE AS PRESENTED IN FIVE REPORTS

Kidney	1	1	1	1	
Spleen	2	2	2	3	2
Liver	3	3	3	2	1
Bladder	4	8	2	4	
Jejunum	5	4	4	1	
Pancreas	6	7			
Colon	7	5			
Duodenum	8	6			
Diaphragm	9				

nal structures. This state of affairs has been called "peritonism." I do not know if this is a good term, but it is used to indicate pseudo-injury to intraabdominal viscera. A hurried decision to perform laparotomy in such a patient must be avoided; careful continued observation of abdominal findings will enable one to avoid unnecessary and unrewarding laparotomy. In doubtful situations paracentesis may be used to detect the presence of blood, bile or intestinal contents.

It is interesting to note the relative vulnerability of the abdominal structures. Data from several reported series are presented in table 8. The kidney was most commonly injured in four series of abdominal injuries. This does not sound familiar or reasonable, but I think the explanation lies in the fact that conservative management for the traumatized kidney usually suffices unless there is massive hemorrhage from a torn renal pedicle or a "shattered" kidney.

X-ray studies often are very useful in cases of abdominal trauma. They may show pneumoperitoneum, fractures, masses, or displacement of hollow viscera by hematomas, although this may occur late. When specifically indicated, cystograms or intravenous pyelograms are helpful in determining damage to the urinary tract. Often the earliest and most important roentgenologic finding is pneumoperitoneum, which is an absolute indication for laparotomy. We are accustomed to the use of an "upright" film or one taken in the lateral decubitus position, but a film which will show pneumoperitoneum can be obtained without

FIGURE 8. This roentgenogram was obtained by placing the x-ray cassette alongside the patient's abdomen while he remained recumbent in his bed after having been brought to the x-ray department. While lacking in some detail, it is entirely adequate to determine the presence or absence of pneumoperitoneum and avoids the manipulation of the patient which "upright" films require.

disturbing a recumbent patient. He can be moved to the x-ray department in his bed, and a cassette placed vertically along his abdomen. A film showing the lateral projection of the abdomen, obtained in this way, may lack some detail but will show the presence or absence of pneumoperitoneum (figure 8). This information may be the most important basis for further management. In the patient whose film is shown in figure 8, it enabled us to stay out of the abdomen and treat him conservatively, a decision which proved to be correct.

Questions and Answers

DR. CURRY: Dr. Oldberg, how should a patient with a head injury be transported? What is your opinion of tracheostomy, and when do you do it? What type of head injury precludes the immediate treatment of other injuries?

DR. OLDBERG: Transportation of a head-injured patient is less important, I expect, than is transportation of a patient with any other kind of injury. Unless there are other injuries such as a spinal fracture, a fracture of a long bone or a visceral injury, the thing to do is to get the patient on an ambulance cot and to the hospital. Transportation really is not a very great problem in a case of a head injury.

Tracheostomy should be performed, as I have already mentioned, if the patient does not have a good airway and if he has a serious injury and there is some impediment to respiration which cannot be corrected by simple methods. It is not difficult to accomplish nowadays compared with what it used to be; in fact, in many hospitals the anesthetic department will do it for you if the nose and throat people are not around. I certainly would want good air exchange for any patient with a serious head injury.

In answer to the question about the severity of a head injury which would preclude other procedures such as repair of abdominal injuries or fractures of long bones, there have been two tremendous advances which I always tell the students about in regard to the treatment of emergency situations anywhere in the body. One is the development of antibiotics. One does not have to operate within a couple of hours, for example, to close a laceration, in order to prevent suppuration; antibiotics can give enough time for it to be done correctly in an operating room. The second advance is the improvement of anesthesia in the last 15 years. Because anesthesia can be so well given, with a good airway and without shock or a limitation of the time necessary to repair the injury, I would say that in most cases of head injury, unless there is extreme shock, one can go ahead with other procedures which seem to be required on an emergency basis. Definitive procedures are, of course, quite a different matter. A reparative procedure that could be put off without harm to the patient certainly should be put off. But an injury that requires immediate care, such as an abdominal injury, a chest injury, or a fracture of a long bone, should be treated as indicated.

I have seen a few automobile accident cases in which there were multiple skeletal fractures as well as a head injury, and these patients are in a state of profound shock and stay that way for quite a long time. It is not just the head injury which produces the shock; a head injury rarely produces prolonged shock. It is the other fractures and injuries which have put the patient in such shock that it is very hard to get him out of it. In that case I think one has to use common sense, and if you know that the least bit of manipulation would be disastrous, naturally you avoid it. I am not too afraid of the head injury itself as far as ordinary situations are concerned.

DR. CURRY: You would subscribe, then, to stabilization of associated long-bone injuries?

DR. OLDBERG: I would, unless they involved all four extremities or there were about six fractures in each leg, or something like that, associated with shock.

DR. CURRY: What would you do then?

DR. OLDBERG: I would apply splints and put the extremities in extension, or whatever was necessary. You probably know more about that than I do.

DR. CURRY: I don't, but that is what I mean by stabilization.

DR. OLDBERG: I would do that much. I would not let the patient lie there with his leg angulated in several different ways.

DR. CURRY: To get back to the first question, about transportation of a head-injured person, do you feel it is better to put the head on the side when the patient is transported, or do you want it upright? Do you put the head over on one side to help get rid of secretions that may accumulate?

DR. OLDBERG: It is all a matter of airway. Yes, patients breathe better if the head is over to one side. I think about the only thing that is important in the transportation of a patient with a serious head injury is to see that the ambulance attendant holds the head in such a way that the patient is breathing easily, whatever position that may be.

DR. CURRY: We have coined a phrase in our hospital about doing tracheostomy "when we think of it." By that I mean that when we have a patient who is badly injured and needs air, if we think of tracheostomy that is when we do it. How do you feel about that?

DR. OLDBERG: I am not a bit afraid of tracheostomy, and I want to be sure the patient gets an airway; and if that is the way to give it, I give him an airway.

DR. KEELEY: I have often thought of tracheostomy as the sort of thing that is done when the question is raised. It is something like standing in front of a mirror, feeling your face,

and wondering if you should shave. If there is any doubt about it, shave! If there is any doubt about doing a tracheostomy, do it. I don't think anything else ensures the airway better than a tracheostomy which is working properly.

DR. OLDBERG: Agreed.

DR. WEISEL: I think tracheostomy is indicated when secretions cannot be cleared by any other method, and I agree with Dr. Keeley and Dr. Oldberg wholeheartedly, but I would add a couple of other indications. In emphysematous elderly patients who are injured, and in very young injured patients, usually tracheostomy is indicated. It is also indicated for the unconscious patient or the one with a chest injury who also has an injury of the neck, jaw and face, and for those patients who require controlled respiration using a positive pressure respirator—so-called intrapulmonary stabilization—when you cannot control the crushed chest by any other means. Tracheostomy, however, is not a procedure to be taken lightly. Afterward, you or somebody else must stay with that patient 24 hours a day.

DR. CURRY: Tracheostomy necessitates some care afterward, does it not?

DR. WEISEL: Yes.

DR. KEELEY: I would certainly think so. Whether or not you do a tracheostomy might depend on the availability of adequate supervision. At times you may be influenced by an uncertainty that the patient is going to be watched closely enough afterward.

DR. CURRY: Dr. Weisel, what type of transportation do you recommend for a patient with a chest injury?

DR. WEISEL: When one of my colleagues asks me about this problem, I usually ask two questions: Is the patient conscious or unconscious? Does he have a crushed chest? If he is unconscious he needs particular attention to his jaw and tongue. Dr. Oldberg already emphasized this point, and I will re-emphasize it. If the patient has a crushed chest, I tell my colleague to transport the patient on his side with the worse side down and the better side up, which we have to leave to him to decide.

DR. CURRY: I think that is excellent advice. What do you do to a flail chest?

DR. WEISEL: Let me describe a patient to illustrate what we do. Three weeks ago a 67 year old man was admitted to our service after having been crushed between a five ton truck and a steel loading platform at a cannery. The foreman, who brought him to the hospital, said that during the ride to the hospital the injured man's respirations became noisy and he "swelled up like a poisoned pup." This patient had subcutaneous emphysema that extended from his scalp to his toes. He was in shock, he was pale, and yet somewhat dusky, and he had paradoxical motion of his entire chest, on both sides. An endotracheal tube was placed in the trachea, secretions were aspirated, intercostal nerve block was performed in the paravertebral area (about at the levels of 2 to 10 on the right and 4 to 8 on the left), and a catheter was placed in the right side of the chest because there was a shift of the apex beat to the left. We then took x-rays and examined the patient more carefully, but at the same time we reassured him that if he breathed and coughed it wouldn't hurt anything inside, and he was taught to rebreathe by expanding the right side of his chest. We feel that most cases of paradoxical respiration in a conscious patient can be handled in this way.

DR. CURRY: Dr. Keeley, here is a question for you. In our audience are physicians from all sections of the country—from small towns, larger towns, perhaps some areas where there are no hospitals. With your excellent ability to philosophize on many important things, would you give us your idea of what a doctor in a small town of several thousand people with no hospital should do when he encounters a case such as the one you described. What should he do for the patient with a head injury, a chest injury, suspected abdominal injury and several fractures of the lower extremities?

DR. KEELEY: I am sure many people in the audience could answer that better than I, but there is one point to remember (and Dr. Curry's experience in Flint bears it out): When there is a disaster, help comes from all directions. The multiple injuries which this patient has are certainly a disaster for him, and I am sure that what should happen is that all the medical talent in the area should be called,

should be utilized to the fullest extent, because many of these compound or multiple injuries cannot be handled by any one doctor. If you do not have a hospital with its interns and residents and other ancillary help, certainly you have to call on your colleagues. This spirit of cooperation is something that expresses itself spontaneously in behalf of the patient, just as it does in a disaster involving many people.

DR. OLDBERG: As an epilogue to those remarks, you know sometimes the medical profession is not very affectionately regarded by the general public, but if they could see the way we rally around when somebody is in trouble, when the patient is in trouble and the doctor taking care of him needs help; if they could see what happens spontaneously every time a situation like that arises, perhaps this would generate a bit of affection for us. I know of no other profession in which real brotherly love and help in time of crisis are demonstrated better than in the practice of medicine.

DR. CURRY: I concur with that, Dr. Oldberg, having lived through a couple of tornadoes. The first one injured a thousand people and killed 116 in two minutes, and a lot of help was needed. It was gratifying and wonderful to see that everyone in the profession instinctively seemed to want to do something without request, and most times they did it right.

Dr. Weisel, do you strap chests?

DR. WEISEL: No.

DR. CURRY: Suppose somebody fractured a couple of ribs out in the country and you didn't have your set to inject something; what would you do? Would you strap him or just let him go and hurt?

DR. WEISEL: Academically I still have to answer no to the question about strapping chests. There may be extenuating circumstances. If a doctor is going to strap a chest because of fractured ribs, I think it is imperative for that same doctor to examine that chest two or three times a day every day until the patient is well, because the danger of atelectasis, hemothorax, and complications that may well threaten the life of that patient is great. We ordinarily say, do not strap chests; it interferes with pulmonary function and oxygenation, and the injury can be handled by other means if you are competent enough to do it.

DR. CURRY: You want the adhesive changed how many times—every two or three days?

DR. WEISEL: The chest should be examined, I should say, but I think the best thing to do is not to put the tape on.

DR. CURRY: Suppose the patient has a hairy chest. Is that going to make any difference?

DR. WEISEL: I think that would influence me, too.

DR. CURRY: Did *you* ever have a broken rib?

DR. WEISEL: Yes, I have.

DR. CURRY: Did somebody strap it?

DR. WEISEL: Yes.

DR. CURRY: Dr. Keeley, you talked about the relative importance of the various injuries we have discussed. If a patient has a head injury, a chest injury, injuries of the abdomen and extremities, which, in your opinion, takes first place?

DR. KEELEY: To answer that, I must repeat what I said before, that you must have a living patient to treat and, of course, the airway comes first. If necessary, we do a tracheostomy and make sure the patient has good respiratory exchange. The next hazard I mentioned was perforated bowel, and the lower down in the bowel it is, the more serious it becomes; the greater the shock and the greater the peritonitis that will result. If, for example, a torn ileum or a perforated colon remains untreated for several hours, irreversible shock may develop. Perforated viscus is, therefore, considered second in importance. Then we come to the open injuries, the fractures, soft-tissue injuries and, of course, we are not going to overlook the head injuries. But, as Dr. Oldberg suggested, the latter should not interfere with the treatment of these other problems.

While you are resuscitating the patient, maintaining an airway, and treating him for shock, there are some injuries you might treat without putting the patient back into shock. This could go on concomitantly with all the resuscitative maneuvers. Dr. Oldberg's statement that a patient who is in shock certainly should not be made worse by manipulation of a long-bone fracture is correct and important.

There is a sequence to follow, but treatment can overlap a little depending on the judgment of the team captain.

DR. CURRY: Dr. Oldberg, have you a classification for craniocerebral injuries that is practical and workable?

DR. OLDBERG: No. I do not think there is any classification for them, unless one wants to classify them as far as fracture of the skull is concerned. One can say there are closed head injuries, head injuries with merely a scalp laceration, compound skull fractures, and depressed skull fractures; each, however, may do more or less harm to the patient, depending on the extent of injury to the brain. Fundamentally it is the brain in which we are interested, not the skull. In a closed head injury, we are interested in restoring the brain to normal function as soon as we can. Probably the classification to use in such a case—and closed head injuries comprise the vast majority of all head injuries—depends a lot on the state of consciousness. People don't seem to understand that. The state of consciousness and the length or duration of the coma following head injury are among the most important things on which to base an evaluation of the damage, plus, of course, any abnormal neurologic findings such as abnormal reflexes or paralysis.

In other forms of injury which involve skull fracture too, we are interested primarily in the possibility of infection. Strangely enough, depressed skull fractures, contrary to the impression so many doctors seem to have, are practically never emergency situations. We do not elevate depressions immediately except once in a blue moon, because they do not occupy enough of the cranial cavity to make it worthwhile to submit the patient to a surgical procedure immediately; we do that electively in a couple of weeks.

Classification other than that is very difficult to make. One classifies the injuries by degree of severity rather than by name.

One term which is used all the time and which is absolutely meaningless is the lawyers' favorite term "concussion." This means only a blow, and when I am asked to define a concussion, such as when the Industrial Commission insists that I give an answer, I tell them it is a head injury of sufficient force to produce momentary unconsciousness. I don't know a better definition than that. Concussion is not a syndrome, in other words, and yet the word is used as though it were, constantly.

DR. CURRY: It seems to me we have asked all the questions we are entitled to ask during the time allotted to us. I am sure all of us agree that we advocate good, safe transportation of injured persons; the ambulance does not need to speed, we have proved that; the injured person deserves a safe ride to the hospital. All of us are charged with the responsibility of immediate recognition of the site, extent and seriousness of the injury and the general condition of the patient, and with proceeding courageously but with balanced and rationalized thinking, doing the best we can for the particular situation.

Most speeches are summarized, and mine is summarized with three words: *Do it now!*

CASE REPORT

Arrhenoblastoma of the Ovary

GILLES BELISLE AND FRANCOIS ROY

Hôtel-Dieu, Quebec

A case of malignant arrhenoblastoma of the ovary in a 62 year old white woman is described. The patient had hirsutism of the face, masculine contours, and enlargement of the clitoris. Postoperative urinary excretion of 17-ketosteroids was 17.33 mg. in 24 hours. Following removal of the tumor, there was no regression of masculinization. The malignant transformation was obvious.

THE designation arrhenoblastoma was coined by Meyer for an ovarian tumor which originates in certain male-directed cells persisting in the ovary from the early stages of gonadogenesis.[1] Alternately it has been suggested that the tumor is of teratomatous origin[2] with differentiation along the lines of androgenic testicular elements. At any rate, the genesis of arrhenoblastomas with their androgenic activity is still controversial.

Arrhenoblastoma is characteristically a tumor of young women, the greatest incidence being between the ages of 20 and 30 years, but it may be found at any age from puberty to postmenopausal life. The tumors tend to have the same gross anatomic features as the granulosa-cell and theca-cell growths and are usually unilateral. About 30 per cent of the tumors recur or metastasize. They vary in size up to a diameter of 15 to 20 cm. The surface is smooth, and the cut surface is grayish and may be solid or may show areas of cyst formations. The cystic degeneration is frequent, with even rather large cystic cavities in the larger tumors.[3-6]

Unless clear clinical evidence of masculinization is present, it is difficult at times to establish the identity of these neoplasms, as they present a great variation in cytologic details. Neoplasms may be classified[4] as follows: (1) a sarcomatoid type showing undifferentiated spindle-cell sarcomatous patterns, (2) an intermediate type with cords or masses of epithelial cells that closely resemble those in granulosa-cell tumor and with abortive tubule formation, and (3) a well-differentiated or adenomatous form with prominent and distinct testicular tubules.

The presence of large eosinophilic polyhedral cells with lipid-containing cytoplasm is helpful for the diagnosis of arrhenoblastoma.

GILLES BELISLE

FRANCOIS ROY

These cells are similar to the Leydig cells of the testicle and are prominent in the intermediate type of arrhenoblastoma.[4,7,8] Moreover, in the majority of cases a very thorough examination will reveal the cordlike arrangement of cells, or imperfect tubule formation, or lipid-containing cell elements, indicating the arrhenoblastomatous nature of the tumor. However, the clinical history is of the greatest value to the pathologist in the microscopic examination of these tumors. This fact can be typically illustrated by sketching the developments of the following case.

Case History

A 62 year old white multipara was admitted at the Hôtel-Dieu in Quebec on July 16, 1958. For two years she had complained of gradually increasing lower abdominal pain and of enlargement of the abdomen. There had been no vaginal bleeding since the age of 52 years, when she had an abrupt menopause with only occasional hot flushes.

On examination, the patient was noted to be of strong nature. Nutrition was good. She weighed 175 lb., but said she thought her weight recently had increased slightly. There was no anemia; the hemoglobin level was 14.5 gm. Blood pressure was 140/70 mm. Hg. Hirsutism was marked, but at this date was not considered excessive for a postmenopausal patient. The abdomen was enlarged, and there was a large, well-defined tumor in the lower abdomen. There was no evidence of free fluid. The patient had had three full-term pregnancies. Digital examination of the cervix with two fingers showed the cervix to be displaced backward; the lower pole of a large cystic swelling could be felt in the anterior fornix. A provisional diagnosis was made of an ovarian cyst, nature unknown. The patient rested in the hospital for two days prior to operation.

Laparotomy was performed on July 18. Anesthesia was induced with PENTOTHAL®, fluothane, ether and curare. A right paraumbilical incision was made. A large tumor was seen arising out of the pelvis. The abdominal peritoneum and greater omentum showed deposits of white flaky material and nodules. The lower pole of the tumor was seen to arise from the right ovary. The pedicle of the tumor was clamped and the tumor was removed. The uterus and left ovary were not removed, because of peritoneal metastasis. The liver appeared to be normal but the gallbladder contained many large calculi. The abdomen was closed. The condition of the patient at the end of the operation was satisfactory. The postoperative course was uneventful, and five days after the operation radiotherapy was begun over the abdomen at a rate of 300 r a day for 12 days. She returned home after 17 days.

When the pathologic report of arrhenoblastoma was received, it was appreciated that not enough attention had been given to masculinizing symptoms and signs, and the following additional details were noted. For four years prior to operation the patient had noticed increased growth of hair on the face and suprapubic region. For two to three years she had been shaving once or twice a week, and immediately prior to admission to the hospital she had been shaving even more frequently. In addition the hair on the forehead fell out and the hairline receded on both sides. Body contours were masculine in type, and the patient admitted that she had a male voice; such change was very apparent to the examiner. There was a slight degree of obesity, particularly of the trunk. The escutcheon was masculine, and the clitoris was markedly enlarged.

The patient was again hospitalized from April 22, 1959, to May 12, 1959, for cobalt therapy to the abdomen; she received 8400 r. A special investigation was made of excretion of 17-ketosteroids during this period; the rate was 17.33 mg. in 24 hours.

The patient was last seen on June 25, 1959,

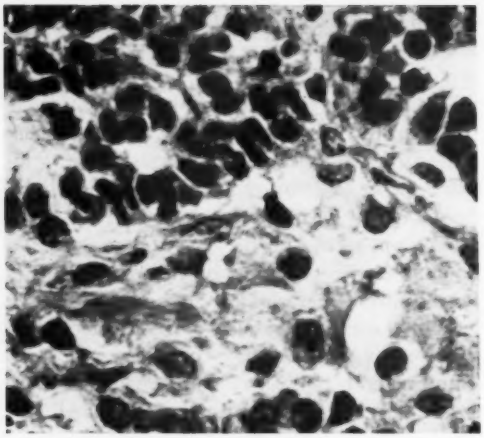


FIGURE 1. Pseudotubular arrangement and interstitial cells (x 720).

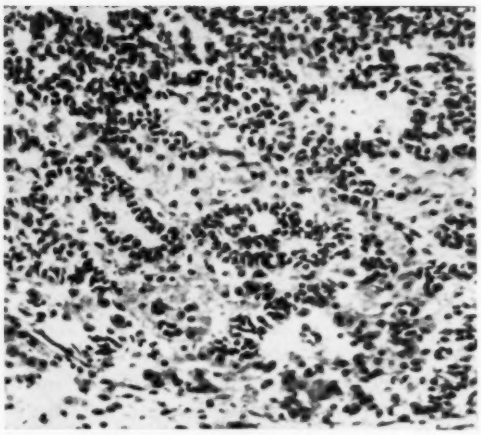


FIGURE 2. Abortive tubule formation, irregular cords and interstitial cells (x 180).

11 months after operation. There was no change in the masculinization. Her usual behavior patterns, including aggressiveness in business administration, were not affected by the removal of the tumor. Prior to operation she had not had vaginal bleeding since the occurrence of menopause, but beginning in February 1959 there had been a small amount of brownish discharge from the vagina daily. The patient had lost 13 lb. in the four or five weeks prior to the time she was seen. The abdomen was still enlarged and a painful resistant mass was felt in the left iliac fossa. The rectal lumen was narrowed at the level of 10 cm. from the anorectal margin. Malignant recurrence was diagnosed.

Gross Findings

The operative specimen consisted of a large cystic tumor weighing 3,110 gm. and measuring 28 by 25 by 15 cm. The cystic cavity was multilocular, some locules containing clear fluid and others containing a slightly turbid brown-red fluid. Many other cystic spaces were filled with sticky, slightly gelatinous fluid. The thickness of the wall varied from 1 to 15 mm.

Microscopic Examination

The walls of many cysts consisted of the neoplastic tissue and of connective tissue; both were present in varying quantities. Sometimes the neoplastic tissue occupied the greater part of the cystic wall, but in other places only thin strands of it were found. The tumor was composed of islands of epithelial cells in the form of lobules separated from each other by strands of connective tissue. The epithelial cells had an irregular tubular arrangement in some areas, and in others they were in the form of cords (figures 1 and 2). The cells were cuboidal in type and often were heaped up to encroach on the lumen and occlude it.

At the periphery of the cellular neoplastic tissue, and sometimes also inside it, there were larger cells of a different type. They had round to oval nuclei with one or sometimes two conspicuous nucleoli and a pink granular protoplasm. The cells were lying singly or in small groups or rows. The specimen of greater omentum submitted showed the same neoplastic pattern.

Discussion

There is little doubt that the tumor was an arrhenoblastoma. The pseudotubular arrangement as well as the irregular cords corresponded almost exactly with most of the cases reported.[1, 7, 9, 10] The interstitial cells were also quite typical. This appearance differs from that of the trabeculae of granulosa-cell tumors,

which consist of several indistinct layers of rounded cells with round nuclei.[4,6]

The degree of masculinization produced by an arrhenoblastoma appears to correspond to the number and development of cells of interstitial Leydig type, which were numerous in this case. In the intermediate type, the degree of masculinization is greater than it is in the sarcomatoid or the well-differentiated form of the tumor. The explanation is that the main source of testicular male hormone is believed to be the interstitial cells of Leydig which are more numerous during fetal development of the testicle before the germinal cords have canalized.[1,3,4,8,11]

In this case, we have also to consider the evidence of malignant transformation. Eleven months after the operation the patient's condition remained about the same as it was prior to operation. Removal of the tumor brought no regression of the symptoms, and recurrence was clinically evident.

REFERENCES

1. Teilum, G.: Classification of testicular and ovarian androblastoma and Sertoli cell tumors. Cancer 4:769-782, 1958.
2. Hartz, P. H.: Giant cystic arrhenoblastoma of the ovary containing entodermal epithelium and a carcinoid. Am. J. Path. 21:1167-1191, 1945.
3. Novak, E.: Gynecologic and Obstetric Pathology With Clinical and Endocrine Relations. Ed. 3. Philadelphia, W. B. Saunders Company, 1952, pp. 423-432.
4. Anderson, W. A. D.: Pathology. Ed. 3. St. Louis, The C. V. Mosby Company, 1957.
5. Robbins, S. L.: Textbook of Pathology. Philadelphia, W. B. Saunders Company, 1957, pp. 1053-1054.
6. Masson, P.: Tumeurs Humaines. Ed. 2. Paris, Norbert Maloine, 1956, pp. 677-680.
7. Spillman, F.: Tubular adenoma (arrhenoblastoma) of the ovary. Am. J. Obst. & Gynec. 25:517, 1933.
8. Warren, S. and Olshausen, K. W.: Interstitial cell growths of the testicle. Am. J. Path. 19:307-331, 1943.
9. Laffargues, P.: Tumeurs mâles de l'ovaire. Presse méd. 63:959, 1955.
10. Hughesdon, P. E. and Fraser, J. T.: Arrhenoblastoma of the ovary. Acta obst. et gynec. scandinav. 32 (supp. 4), 1953.
11. Kanter, A. E. and Keawans, A. H.: Arrhenoblastoma of the ovary. Am. J. Cancer 40:474-484, 1940.

Postgraduate Clinical NOTES

143. CESAREAN SECTION

A more logical approach has been formulated to the delivery of the baby. Delivery through the birth canal is the most desirable objective; but it is no longer justified at any price. It is possible to evaluate the size of the pelvis rather accurately, and the final decision as to whether the baby can be delivered safely through the birth passages may await an intelligent test of labor. The length of the test of labor is less important today than a careful evaluation of progress. In the final decision to terminate the labor by cesarean section one should give careful consideration to the fact that once a cesarean section is carried out future deliveries will most likely be accomplished by the abdominal route. Thus the indication for the performance of the initial cesarean operation is of paramount importance for the patient's future childbearing.

M. Edward Davis, Progress in the management of labor and delivery, *Journal of the American Medical Association*, January 30, 1960, pp. 409-413

CLINICAL STUDY

Diuretic Evaluation of Chlorazinal

MORTON FUCHS, WILLIAM WILSON,
SANFORD R. MALLIN AND LETICIA HERNANDO*

Hahnemann Medical College and Hospital, Philadelphia

The average weight loss after 48 hours in 14 ambulatory cardiac patients receiving chlorazinal was 1.6 lb., comparing favorably with the response to other oral diuretics. Determinations of blood urea nitrogen and creatinine levels and urinalyses in 29 patients receiving the drug indicated that it tends to increase blood urea and to increase cellular content and casts in the urine in certain patients; an exception was a patient with acute glomerulonephritis in whom the blood urea decreased.

MORTON FUCHS

THE discovery by Lipschutz[1,2] in 1944 of the triazine derivatives and their diuretic properties stimulated investigators to study this new group of substances clinically. Chlorazinal (N-para-chlorophenyl 1-2, 4-diamino-5-triazine hydrochloride), a triazine derivative which previously has been reported to possess remarkable diuretic effects with little toxicity, also has proved to be an effective nonmercurial diuretic agent when administered orally. Ford and associates[3] demonstrated clinically in man and in laboratory animals (dogs) its effects on renal hemodynamics and on water and electrolyte excretion. In dogs, urinary excretion of water and sodium rose significantly and the glomerular filtration rate decreased slightly following the intravenous administration of chlorazinal hydrochloride (DAQUIN®). The same effects were observed in human subjects after the drug was administered orally. It has been noted that the effective range of dosage is 300 to 600 mg. daily. The drug's action is manifested two hours after oral administration and persists for 18 hours. Comparison with other diuretics has shown it to be equivalent in potency to

*Department of Medicine, Hahnemann Medical College and Hospital, Philadelphia, Pennsylvania.

TABLE 1

ACUTE 48 HOUR WEIGHT RESPONSE IN 14 PATIENTS RECEIVING 150 MG. OF CHLORAZINAL TWICE DAILY*

PATIENT	WEIGHT (POUNDS)	
	Before drug	*After drug*
K. G.	131.5	132.8
M. W.	195.8	192.8
E. W.	236.0	234.5
F. A.	151.0	149.5
S. C.	112.0	109.5
N. Mc.	170.5	168.2
M. W.	163.0	159.0
N. L.	119.5	118.5
C. S.	130.2	130.0
N. P.	127.0	122.0
E. B.	100.0	99.0
L. M.	169.0	167.5
J. S.	163.0	163.8
L. G.	115.5	113.8
Average	148.8	147.2

*Average weight loss 1.6 lb. ($p = <0.01$); no side effects were noted.

chlormerodrin (NEOHYDRIN®) and less potent than either chlorothiazide (DIURIL®) or meralluride (MERCUHYDRIN®).

The present study includes an evaluation of the effects of chlorazinal hydrochloride (Daquin) on urinary findings and on blood urea nitrogen levels and weight loss.

Method and Material

Acute diuretic response to chlorazinal was determined by the weight loss observed in 14 ambulatory outpatients in our Diuretic Clinic, all of whom had arteriosclerotic heart disease and mild to moderate congestive heart-failure and had required weekly injections of a mercurial diuretic to remain edema-free. All patients were receiving digitalis. Control weights were obtained by withholding diuretics for two weeks; other medications the patients were receiving were continued. The patients were evenly divided between the sexes. Their diets and intake of salt were not controlled, as they were all outpatients. They were weighed before breakfast and after voiding. Chlorazinal then was administered in a dosage of 150 mg. twice daily for two days, and they were again weighed. Because previous investigations indicated that administration of this drug may produce an elevation of blood urea levels, an attempt was made to evaluate this phenomenon by continuing the administration of chlorazinal for two weeks and comparing blood urea and creatinine levels before and at the end of its administration.

In addition to this group of 14 patients, 16 patients on the medical ward were given chlorazinal, 150 to 300 mg. twice daily, for one to four weeks. Blood urea and creatinine levels were determined and urinalyses done before and after its administration.

Results

Acute response—The average weight loss after the administration of 150 mg. of chlorazinal twice daily to 14 patients for two days was 1.6 lb. ($p = <0.01$) (table 1). Several other oral diuretic agents were given to the same group of patients for comparison of weight response: chlorothiazide, 500 mg. twice daily; flumethiazide, 800 mg. twice daily; chlormerodrin, 20 mg. four times daily; isobutamide, 250 mg. twice daily; and acetazolamide, 250 mg. twice daily. The response to chlorazinal compared favorably with the response to the other oral diuretics that were used (table 2).

During the period of study to determine the acute response, no side effects were observed

TABLE 2

COMPARATIVE WEIGHT RESPONSE TO SEVERAL ORAL DIURETICS

DRUG	WEIGHT LOSS (POUNDS)	P VALUE
Chlorothiazide, 500 mg. b.i.d.	2.31	$p = <0.001$
Flumethiazide, 800 mg. b.i.d.	2.33	$p = <0.001$
Chlormerodrin, 20 mg. q.i.d.	1.60	$p = <0.001$
Isobutamide, 250 mg. b.i.d.	2.1	$p = <0.01$
Acetazolamide, 250 mg. b.i.d.	2.2	$p = <0.02$
Chlorazinal hydrochloride, 150 mg. b.i.d.	1.6	$p = <0.01$

TABLE 3

BLOOD UREA AND CREATININE LEVELS, 14 AMBULATORY CARDIAC PATIENTS, BEFORE AND AFTER ADMINISTRATION OF 150 MG. CHLORAZINAL TWICE DAILY FOR TWO WEEKS

PATIENT	BLOOD UREA NITROGEN (MILLIGRAMS PER CENT)		CREATININE (MILLIGRAMS PER CENT)	
	Before	*After*	*Before*	*After*
K. G.	24.5	21.2	2.6	2.1
M. W.	11.1	12.3		
E. W.	15	17.8	1.8	1.8
F. A.	9.6	11.3	1.2	1.6
S. C.	13.8	21.8	1.6	1.8
N. Mc.	12.3	7.5	1.2	1.8
M. W.	7.5	6.4	1.2	2.0
N. L.	23.2	23	2.4	2.4
C. S.	27	30	2.6	2.0
N. P.	12	15		
E. B.	10	10		
L. M.				
J. S.	10.9	16.2	1.8	2.6
L. G.	18.2	10		
Average	15.0	15.5	1.8	1.7

and there was no change in blood pressure. All patients in the group were normotensive.

Effect on blood urea levels—The 14 ambulatory cardiac patients continued to receive 150 mg. of chlorazinal twice daily for two weeks. Blood urea and creatinine levels were determined before and after its administration (table 3). Blood urea levels were obtained in 13 patients, and creatinine levels in nine. The average blood urea nitrogen level was 15 mg. per cent initially and 15.5 mg. after two weeks' administration of chlorazinal. The average creatinine level was 1.8 mg. per cent before and 1.7 mg. per cent after therapy. There was no influence on blood levels, and side effects were not noted during this phase of the study. The patients showed good cardiac compensation both subjectively and by physical examination during the two week period.

Four patients on the medical ward were given 150 mg. of chlorazinal twice a day and four others received 300 mg. twice a day for one week. Side effects were not observed (table 4). There was no history or overt physical or laboratory evidence of active, acute or chronic renal disease in these patients. However, patient F. M. had marked debilitation with unresolved pneumonia. Tuberculosis was suspected but could not be proved, and the patient died several days after use of the drug was discontinued. His course had progressed downhill for several weeks, and his death probably was unassociated with administration of the drug. However, the blood urea and creatinine levels did rise acutely after chlorazinal was started. There appeared to be a general tendency for mild elevation of the blood urea in these patients with both dosage levels, and for an increase in white blood cells and casts in the urine after one week of therapy.

The next group of eight patients had various pathologic processes. Seven received 300 mg. of chlorazinal twice daily and one received 150 mg. twice daily for two to four weeks. A summary of each case in this group follows.

Patient F. M.—Daquin, 300 mg. twice daily, was started November 6, 1958 and continued through November 29. Control blood urea nitrogen levels were 12 mg. (October 15) and 10 mg. (October 30). During approximately three weeks of therapy, the blood urea nitrogen levels were: November 19, 16 mg.; November 26, 12 mg.; November 27, 13 mg. Urinalysis revealed the presence of white blood cells, which persisted during the course of therapy; red cells were not noted at any time.

TABLE 4

BLOOD UREA AND CREATININE LEVELS, EIGHT HOSPITAL PATIENTS WITHOUT KNOWN CARDIAC OR RENAL DISEASE, BEFORE AND AFTER RECEIVING CHLORAZINAL FOR ONE WEEK

PATIENT AND DOSAGE	BLOOD UREA NITROGEN (MILLIGRAMS PER CENT)		CREATININE (MILLIGRAMS PER CENT)		URINE CHANGES
	Before	*After*	*Before*	*After*	
B. S. (150 mg. b.i.d.)	21	10	2.2	2.1	Increase in white blood cells and granular casts. Normal control
C. S. (150 mg. b.i.d.)	12	30	1.9	2.4	No change. Normal
A. C. (150 mg. b.i.d.)	9	16	2.1	1.4	Increase in white blood cells and cellular casts. Normal control
F. M. (150 mg. b.i.d.)	9	58	2.4	5.8	Increase in white and red blood cells and coarsely granular casts. Normal control
J. G. (300 mg. b.i.d.)	12	10	2.4	2.1	No change. Normal
J. G. (300 mg. b.i.d.)	12	14	2.1	2.0	No change. Normal
L. S. (300 mg. b.i.d.)	13	25	2.8	2.1	No change. Normal
A. K. (300 mg. b.i.d.)	12	21	2.1	2.5	Increase in white blood cells and many coarsely granular casts. Normal control

Patient L. B.—Daquin, 300 mg. twice daily, was started October 30, 1958 and discontinued November 29. The control blood urea nitrogen level was 14 mg. On November 29 it was 58 mg. and Daquin was discontinued. Four days later the blood urea nitrogen level was 94 mg. A week later, on December 10, it had dropped to 30 mg. This patient has Hodgkin's disease and it is difficult to determine whether or not the changes in the blood urea nitrogen levels could be ascribed to the disease. The sharp drop which followed discontinuation of the drug suggests that it accounted for the changes. No collateral urinary changes were observed.

Patient S. D.—Daquin, 300 mg. twice daily, was started October 31, 1958 and discontinued on November 13. This patient had diabetic acidosis with renal insufficiency when he was admitted to the hospital on October 25, and the blood urea nitrogen level was 92 mg. By October 31 the level had dropped to 35 mg., and Daquin was started on that day. The diabetes continued to be well regulated. On November 7 the blood urea nitrogen level was 52 mg., and by November 12 it had risen to 63 mg. Daquin was discontinued on November 13. By November 16 the blood urea nitrogen level had dropped to 15 mg., and on November 21 it was 13 mg. It appears that the rise in blood urea nitrogen was due to administration of chlorazinal, since the level dropped rapidly to normal values after the drug was stopped. This seems to be a toxic type of derangement, since renal damage of this degree, manifested by a blood urea nitrogen level of 63 mg., would not have reversed so rapidly after the drug was discontinued. If anything, this suggests enzymatic inhibition or perhaps renal vascular inhibition.

Patient L. R.—Daquin, 300 mg. twice daily, was started October 3, 1958 and discontinued November 4. The control blood urea nitrogen level was 10 mg. When the drug was stopped

the level was 15 mg. Thus there was no evidence of renal damage prior to administration of chlorazinal and no change occurred as a result of therapy.

Patient H. D.—Daquin, 300 mg. twice daily, was started on October 31, 1958 and discontinued on November 15. There was no evidence of renal damage prior to institution of the therapy, and there was no rise in blood urea nitrogen during its administration. Control blood urea nitrogen levels were 15 mg. (October 4) and 23 mg. (October 31). The drug was started on October 31, and on November 7 the blood urea nitrogen level was 16 mg. and on November 14 it was 17 mg.

Patient M. Mc.—This patient had acute glomerulonephritis. Prior to administration of chlorazinal there was 4 plus proteinuria with 80 to 90 red blood cells and 8 to 10 white blood cells per high-power field in the urine. Chlorazinal, 300 mg. twice daily, was started November 2, 1958 and discontinued November 21. Before the drug was given, the blood urea nitrogen level was 36 mg., and despite the high dosage of chlorazinal the level dropped progressively. As the glomerulonephritis improved, the levels of blood urea nitrogen were as follows: November 8, 11 mg.; November 9, 9 mg.; November 15, 10 mg.; November 20, 18 mg.

Patient B. K.—This patient had a renal tumor. Chlorazinal, 150 mg. twice daily, was started November 1, 1958 and continued through November 8. The blood urea nitrogen level prior to therapy was 9 mg., and after one week of administration of the drug it was 11 mg. There were no changes in the formed elements in the urine or in the patient's clinical status.

Patient T. C.—Chlorazinal, 300 mg. twice daily, was started November 8, 1958 and continued through November 21. Prior to therapy the blood urea nitrogen level was 10 mg.; after therapy it was 21 mg. No changes were observed in the urine.

The findings in this group of cases suggest that chlorazinal has an effect on blood urea nitrogen levels in the presence of renal damage. It may, in addition to producing an elevation of blood urea nitrogen, also tend to produce increased cellular content and casts in the urine. When there was no apparent overt renal damage, however, blood urea nitrogen levels and urinary findings remained unchanged. By contrast, a patient with acute nephritis exhibited marked improvement while receiving chlorazinal, presumably attributable to natural healing of the renal process.

Discussion

The pharmacologic properties of the triazine derivatives have been discussed in other reports.[1,4-6] Chlorazinal hydrochloride (Daquin), the latest of these compounds and one which produces the least toxicity, has been studied both clinically and in laboratory animals (dogs) in regard to its effect on renal hemodynamics and urinary excretion of water and electrolytes.[3] Earlier investigators have concluded that this drug is a moderately effective nonmercurial oral diuretic agent whose action differs from that of mercurials, carbonic anhydrase inhibitors, and chlorothiazide.[3]

Our studies with chlorazinal (Daquin) confirm the moderate effectiveness of the drug as an oral diuretic agent. The most significant side effect noted was an increase in blood urea nitrogen in some patients. It appears that this elevation occurs mostly in patients with renal damage; the exception was a patient with acute glomerulonephritis in whom the blood urea nitrogen level fell progressively during the administration of chlorazinal. It was also noted that there was a concomitant increase in cellular content and number of casts in the urine of the patients whose blood urea nitrogen levels increased and in some patients whose blood urea levels were unaffected.

Recently we[4] reported that prolonged administration of the thiazide derivatives, including chlorothiazide, brought about an elevation of blood urea levels which may be due to the decreased glomerular filtration rate resulting from progressive dehydration and hyponatremia. Another possible cause is an increase in protein breakdown induced by these agents. The presence of renal impairment would accentuate the rise in blood urea nitrogen levels with either the thiazide or the triazine group of drugs.

The weight response to chlorazinal compared favorably with that to other diuretics, but the possibility of renal toxicity must be kept in mind in the use of this drug.

REFERENCES

1. Lipschutz, W. L., Hadidian, Z. and Kerpesar, A.: Bioassay of diuretics. J. Pharmacol. & Exper. Therap. 79:97, 1943.
2. Lipschutz, W. L. and Hadidian, Z.: Amide, amines and relative compounds as diuretics. J. Pharmacol. & Exper. Therap. 81:84, 1944.
3. Ford, R. V., Rochelle, J. B. and Spurr, C.: Laboratory and clinical observations on chlorazinal hydrochloride (Daquin). Am. J. Cardiol. 3:148, 1959.
4. Fuchs, M. and Mallin, S. R.: A review of the pharmacology of the thiazide derivatives. (To be published.)
5. LeSher, D. A. and Shideman, F. E.: The influence of 2 amino-4-(p-chloroanilino)-s-triazine on the renal excretion of water, potassium and sodium by the rat and the dog. J. Pharmacol. & Exper. Therap. 116:38, 1956.
6. Williamson, H. E., Shideman, F. E. and LeSher, D. A.: Antagonism of the effects of certain steroids on the renal excretion of water and electrolytes by 2-amino-4-(p-chloroanilino)-s-triazine. J. Pharmacol. & Exper. Therap. 126:82, 1959.

Books Received

Books received are acknowledged, and, as space permits, those of principal interest to our readers are reviewed more extensively. Reviews appear in this issue starting on page A-172; additional listings are on pages 703 and A-178.

Medical Care of the Adolescent. By J. Roswell Gallagher, M.D., Chief of the Adolescent Unit, The Children's Hospital Medical Center, Boston. 369 pages, illustrated. 1960, Appleton-Century-Crofts, Inc., New York. $10.00.

Practical Proctology. By Louis A. Buie, Sr., M.D., Emeritus Member, Section of Proctology, Mayo Clinic, Rochester, Minnesota. Ed. 2. 737 pages, illustrated. 1960, Charles C Thomas, Springfield, Illinois. $22.50.

Virus Virulence and Pathogenicity. Ciba Foundation Study Group. Edited by G. E. W. Wolstenholme, O.B.E., and Cecilia M. O'Connor, B.Sc. No. 4. 114 pages, illustrated. 1960, Little, Brown & Company, Boston. $2.50.

Treatment of Urinary Lithiasis. Edited by Arthur J. Butt, M.D., Attending Urologist, Baptist Hospital, Pensacola, with 32 contributors. 577 pages with 189 illustrations. 1960, Charles C Thomas, Springfield, Illinois. $21.00.

From Fish to Philosopher; the Story of Our Internal Environment. By Homer W. Smith, Physiologist. 304 pages, illustrated. 1959, Ciba Pharmaceutical Products, Inc., Summit, New Jersey, with permission of Little, Brown & Company, Boston. $4.75.

Microchemical Methods for Blood Analysis. By Wendell T. Caraway, Ph.D., Biochemist, Flint Medical Laboratory, Flint, Michigan. 109 pages. 1960, Charles C Thomas, Springfield, Illinois. $5.25.

Psychosomatic Methods in Painless Childbirth; History, Theory and Practice. By L. Chertok, Paris, France. Translated by Denis Leigh, M.D., The Maudsley Hospital, London, England. Ed. 2. 260 pages. 1959, Pergamon Press, Inc., New York. $6.50.

Diagnosis and Treatment of Diseases of the Trachea and Bronchi. American Lecture Series. By Herman J. Moersch, M.D. and Howard A. Andersen, M.D., Section of Medicine, Mayo Clinic and Mayo Foundation, Rochester, Minnesota. 108 pages with 35 illustrations. 1960, Charles C Thomas, Springfield, Illinois. $4.25.

Recent Advances in Surgery. Edited by Selwyn Taylor, F.R.C.S., Surgeon, King's College Hospital, London, England, with 28 contributors. Ed. 5. 500 pages with 160 illustrations. 1959, Little, Brown & Company, Boston. $13.00.

Peripheral Facial Palsy; Pathology and Surgery. By Karsten Kettel, M.D., Chief Surgeon, Department of Otorhinolaryngology, Frederiksborg Central Hospital, Hillerd, Denmark. 341 pages with 127 illustrations. 1959, Charles C Thomas, Springfield, Illinois. $19.50.

Outline of Orthopaedics. By John Crawford Adams, M.D., Consultant Orthopaedic Surgeon, St. Mary's Hospital Medical School, London, England. Ed. 3. 440 pages with 313 illustrations. 1960, E. & S. Livingstone Ltd., Edinburgh and London. Distributed by The Williams & Wilkins Company, Baltimore. $8.00.

Clinical Medicine and the Psychotic Patient. By Otto F. Ehrentheil, M.D., Physician, and Walter E. Marchand, M.D., Chief, Medical and Surgical Service, Veterans Administration Hospital, Bedford, Massachusetts, with 12 contributors. 383 pages, illustrated. 1960, Charles C Thomas, Springfield, Illinois. $10.75.

Significant Trends in Medical Research. Ciba Foundation Tenth Anniversary Symposium. Edited by G. E. W. Wolstenholme, O.B.E., Cecilia M. O'Connor, B.Sc. and Maeve O'Connor, B.A. 356 pages with 41 illustrations. 1960, Little, Brown & Company, Boston. $9.50.

Therapeutic Nutrition With Tube Feeding. By Morton D. Pareira, M.D., Associate Professor of Surgery, Washington University School of Medicine, St. Louis. 58 pages, illustrated. 1959, Charles C Thomas, Springfield, Illinois. $3.75.

Postgraduate Medicine

SCIENTIFIC EXHIBIT

Facial Pain

ARNOLD P. FRIEDMAN
CHARLES A. CARTON
ASAO HIRANO

Headache Unit and Divisions of Neurology and Neurosurgery, Montefiore Hospital, New York, New York

INTRODUCTION

FACIAL pain is a symptom which may be associated with a variety of clinical conditions. The underlying disorder may be anatomic, physiologic or psychologic. Although methods affording relief have been found, the basic cause and mechanisms producing the pain, in most instances, remain unsolved. To the patient, such a symptom is disturbing not only because of the unpleasant quality of sensation but because of possible unpleasant psychologic connotations. For the physician, precise diagnosis and treatment of facial pain usually are quite difficult because of the extremely complex cranial and cervical innervation, the intricate vascular supply, and the extent to which the emotional state modulates responses to a painful stimulus.

For purposes of clinical management we can group facial pain into three main categories: (1) typical neuralgias, primarily neurogenic; (2) atypical neuralgias, primarily vascular and psychogenic; and (3) facial pain secondary to other extracranial and intracranial causes. Such a classification has defects but allows a rational approach to diagnosis and therapy.

The Typical Neuralgias

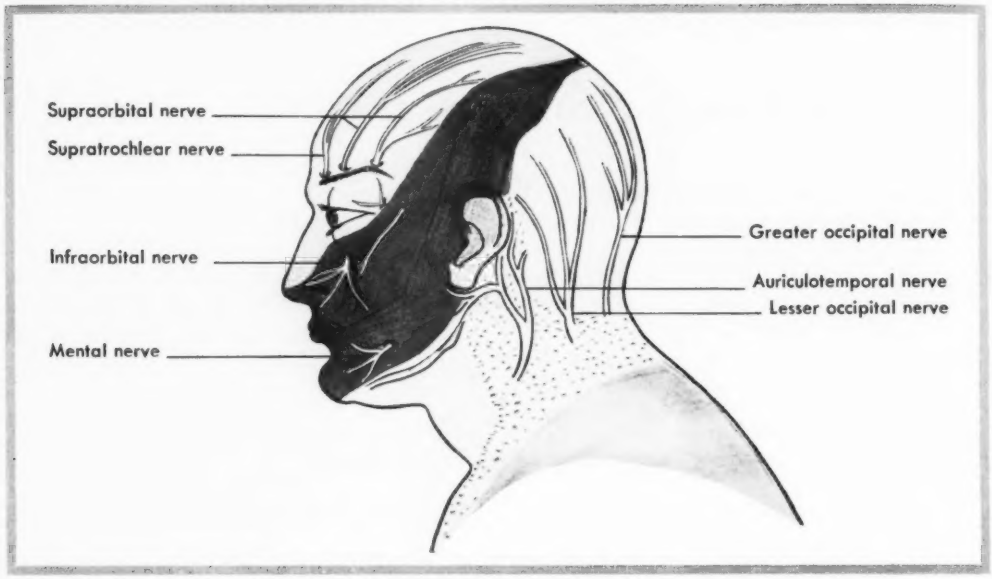
Criteria of the Typical Neuralgias

A typical neuralgia is a paroxysmal, sharp, shooting pain of short duration, with no pain present between attacks, occurring within the sensory distribution of one of the cranial nerves. By definition, it is relieved by temporary anesthetization of the sensory area in which it occurs, or permanently by surgical denervation of that area.

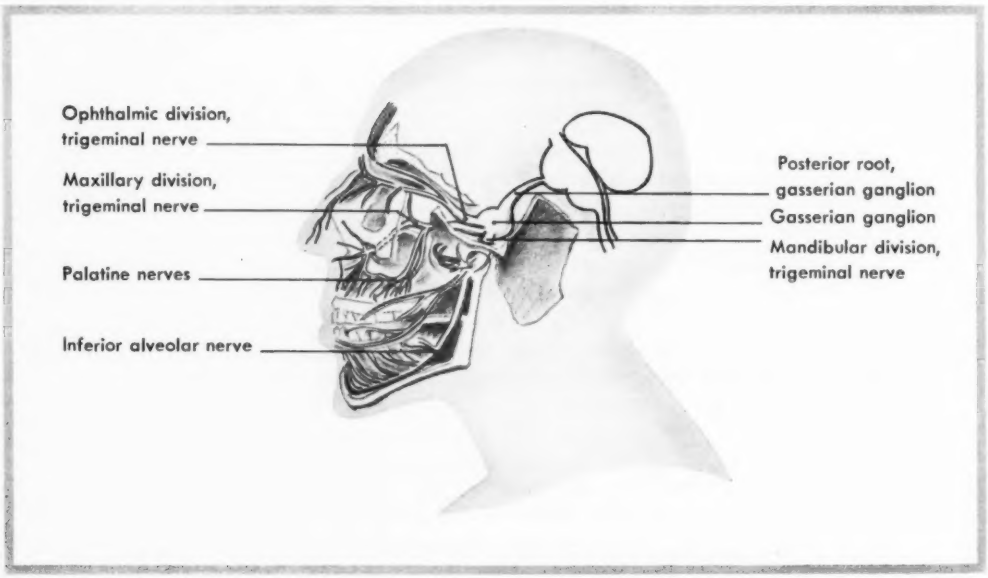
Distribution of pain	Limited in the field of one of the cranial nerves
Character of pain	Paroxysmal, sharp, localized
Duration of pain	Seconds to minutes
Autonomic nervous system signs	None
Precipitation by external stimuli	Yes
Trigger zone	Present
Age	Older age group
Pharmacology	
Vasoconstrictor	No relief
Vasodilator	Inadequate relief
Narcotics	Inadequate relief
Relief by surgical or chemical interruption of cranial nerve	Relief
Personality	Neurotic traits not prominent

Anatomy of Cranial Nerves V and C2

Cutaneous distribution

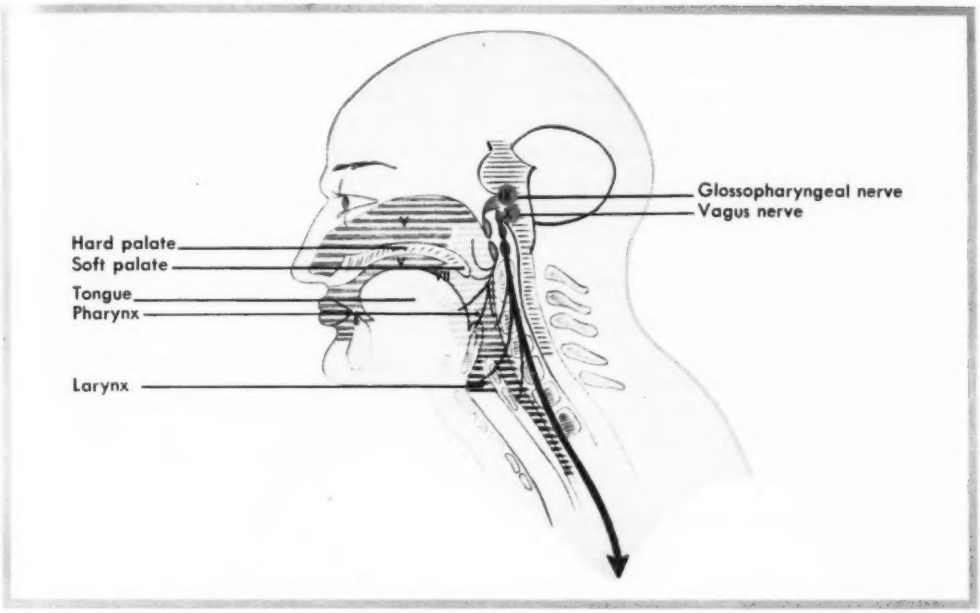


Detailed fifth nerve distribution

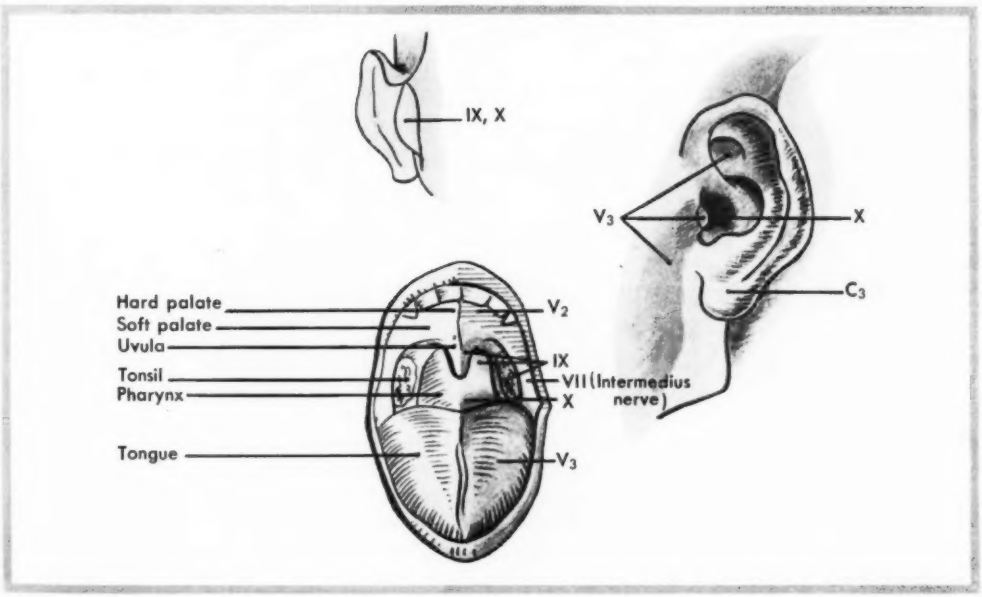


Anatomy of Cranial Nerves V, VII, IX, X

IX, X: Sagittal section



Ear, oropharynx



Specific Characteristics of the Typical Neuralgias

Trigeminal Neuralgia

Pain usually occurs in the second and third divisions of the fifth nerve. Less frequently it occurs in the first division. All three divisions may be involved. There may be trigger areas where stimulation may set off a paroxysm of pain; touch, chewing or swallowing may act as a trigger mechanism. Neurologic examination yields findings completely within normal limits. Specifically, there are *no* sensory changes in the distribution of the fifth nerve.

Occipital Neuralgia

Paroxysmal pain occurs in the back of the head, radiating from the lower part of the neck over the scalp. Pain is limited to the distribution of the lesser and greater occipital nerves.

Glossopharyngeal Neuralgia

Pain usually occurs in the tonsillar area and ear, in the distribution of the glossopharyngeal nerve (IX). It is knifelike, paroxysmal, and often precipitated by yawning and swallowing (liquid and food in contact with appropriate area).

Geniculate Neuralgia

Paroxysmal, stabbing pain occurs deep in the ear. It is not precipitated by swallowing. It may be reproduced by stimulation of the nervus intermedius during surgery.

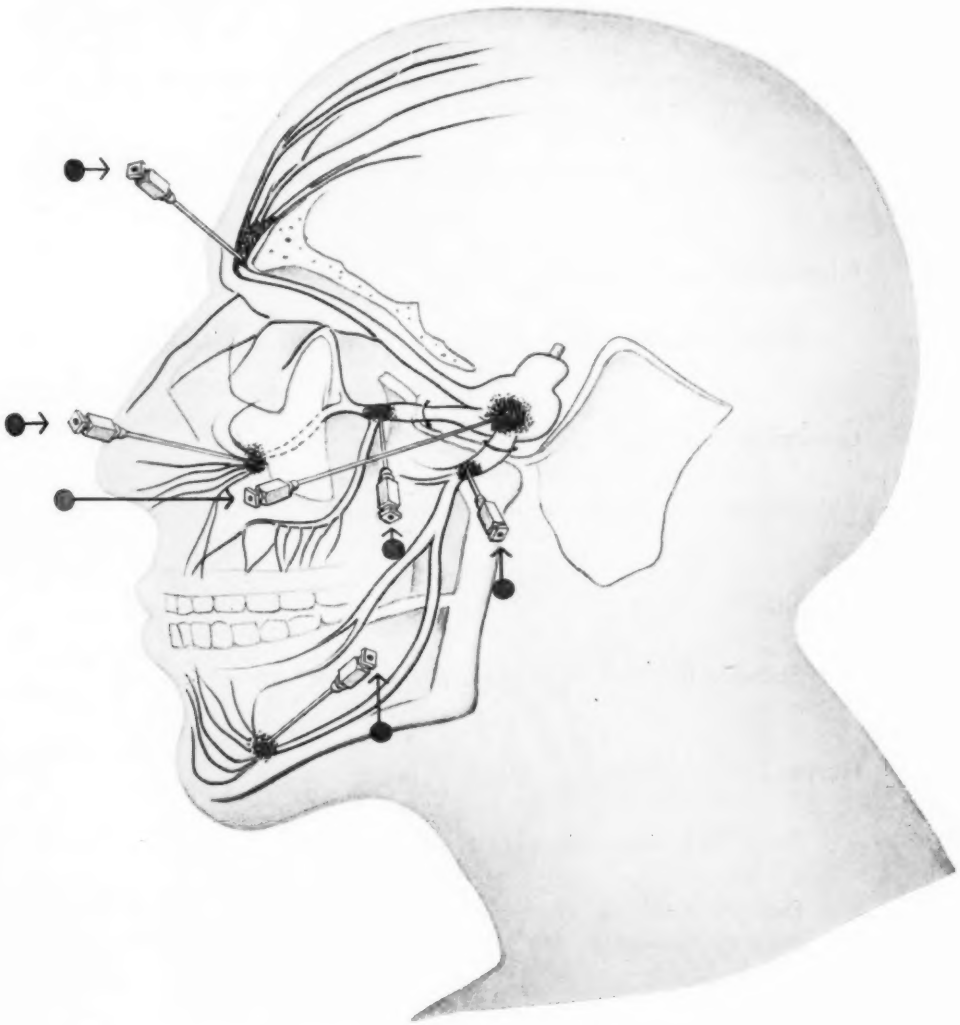
Nerve Blocks for Diagnosis and Therapy

Diagnostic Blocks

Local anesthetic agents may be used to block branches of the fifth nerve. This may be done peripherally in the skin at trigger points, or at the supraorbital, infraorbital and mental foramens. Lingual nerve block may relieve attacks of pain in the tongue. More proximally, nerve blocks at the exiting foramens from the skull will block the maxillary and mandibular divisions. Finally, gasserian ganglion block may be accomplished via the foramen rotundum.

Therapeutic Blocks

Permanent interruption of peripheral branches may be accomplished by alcohol injection at the peripheral foramens, into the maxillary and mandibular divisions at the base, and by gasserian ganglion injection. There may be regeneration of fibers with peripheral injection, but not with gasserian ganglion injection. Cocainization of the tonsillar area will relieve the pain of glossopharyngeal neuralgia.



Operative Therapy

Trigeminal Neuralgia

1. Peripheral nerve avulsion or section.

2. Differential or complete section of the posterior root of the gasserian ganglion, sparing the motor root.
   a. Temporal approach.
   b. Posterior fossa approach.

3. Ganglion decompression, or compression. Both temporarily relieve pain, probably dependent on ganglion cell damage.

4. Section of the tract of the descending fifth nerve in the medulla.

Glossopharyngeal Neuralgia

Section of the ninth nerve and upper vagus rootlets intracranially.

Geniculate Neuralgia

Section of the nervus intermedius intracranially.

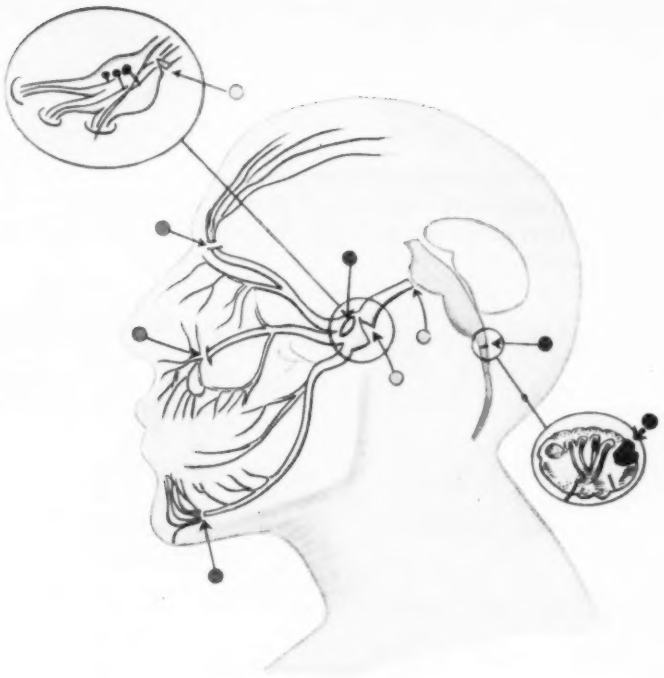
Occipital Neuralgia

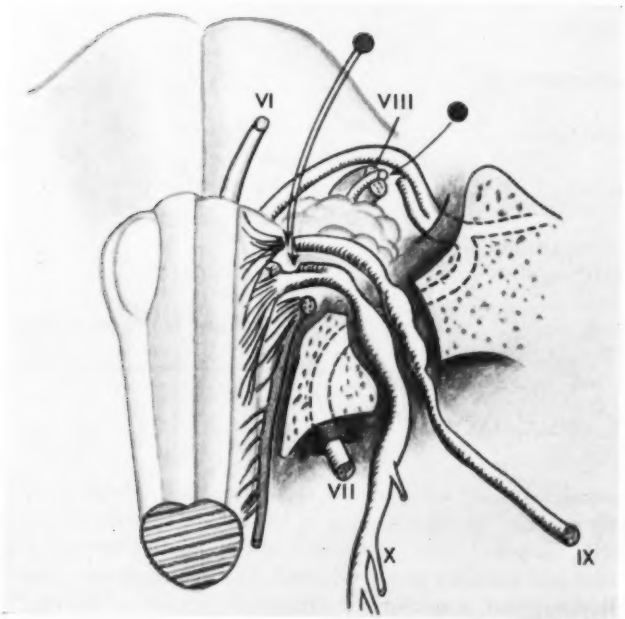
Section of the greater or lesser occipital nerve, or both, extracranially.

Herpes Zoster

Nerve blocks and nerve section do *not* relieve pain.

Elevation of skin flap (from periosteum outward) with repositing of flap *may* relieve pain (skin flap must include postherpetic scars).




VI
VIII
VII
X
IX

Atypical Neuralgias

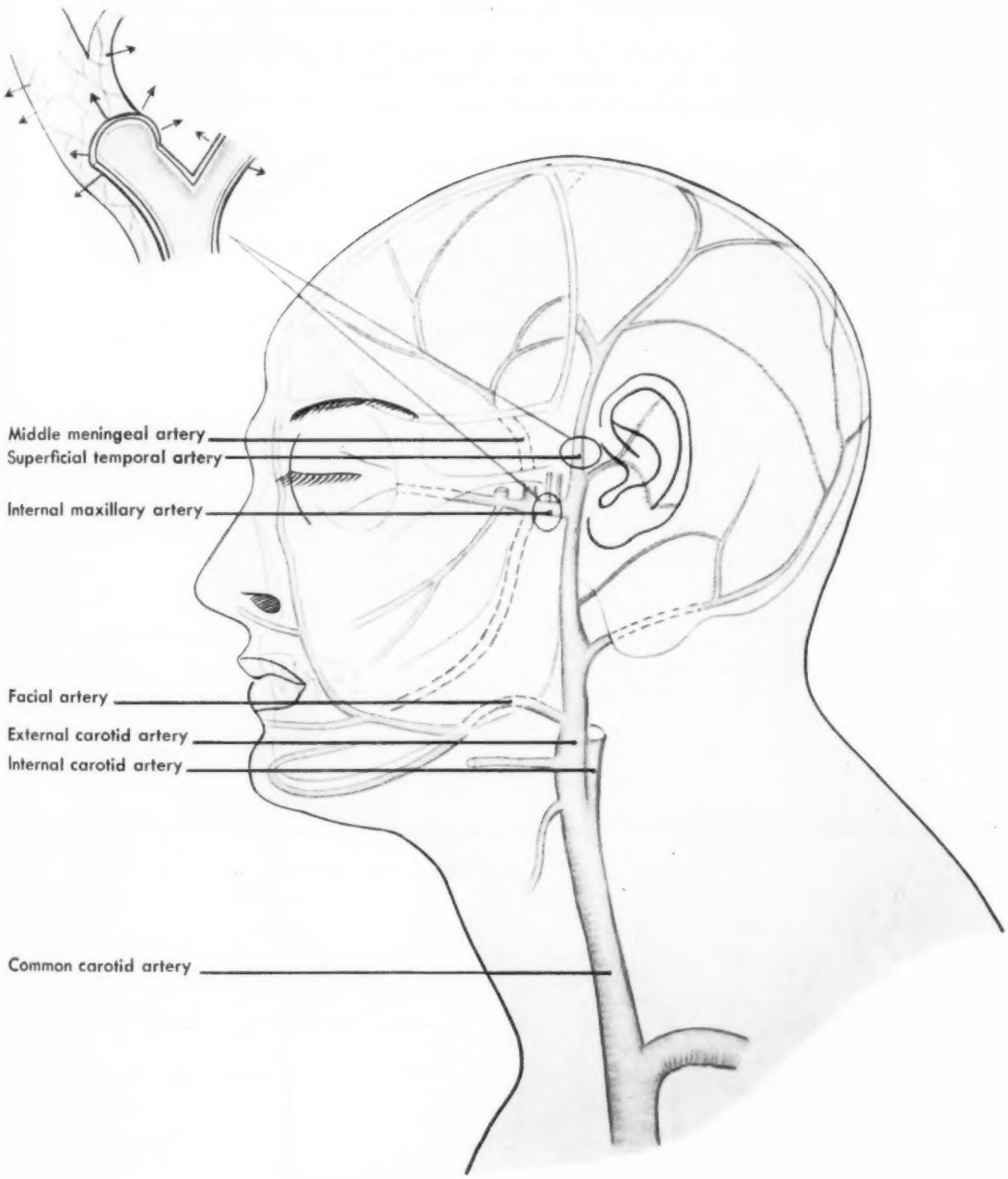
Criteria of Atypical Neuralgias

Atypical neuralgias are characterized by attacks of pain in the head, face and neck which are not well localized and which may occur in paroxysms or be continuous. They frequently are associated with cranial autonomic activity on the side of the pain and often are seen in tense, anxious persons.

Distribution of pain	Does not follow nerve distribution
Character of pain	Diffuse, deep-seated, poorly localized, described as pulling, gripping, etc.
Duration of pain	Hours or days
Autonomic nervous system signs	Lacrimation, flushing, nasal congestion, other symptoms
Precipitation by external stimuli	No
Trigger zone	Absent
Age	Younger age group
Pharmacology	
Vasoconstrictor	Frequent relief
Vasodilator	No relief
Narcotics	Frequent relief
Relief by surgical or chemical interruption of cranial nerve	No relief
Personality	Neurotic traits prominent

Anatomy of Cranial Arteries

In atypical neuralgias, there are periodic attacks of local dilatation of extracranial vessels in areas mainly supplied by the branches of the external carotid arteries, i.e., internal maxillary, superficial temporal. Some terminal branches of the internal carotid artery in the areas of the nose and eye also may be dilated. The fact that one artery or set of arteries may be involved suggests a neurogenic origin.


Middle meningeal artery
Superficial temporal artery
Internal maxillary artery
Facial artery
External carotid artery
Internal carotid artery
Common carotid artery

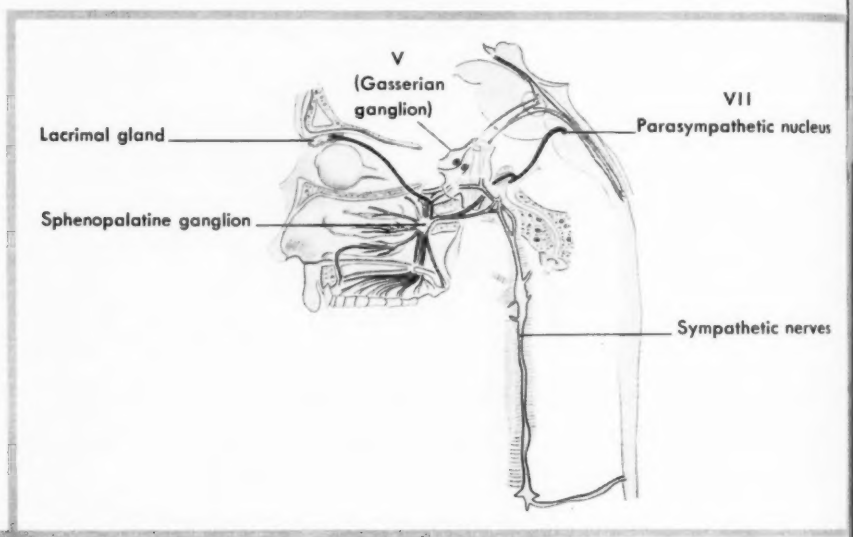
Cranial Autonomic Pathways

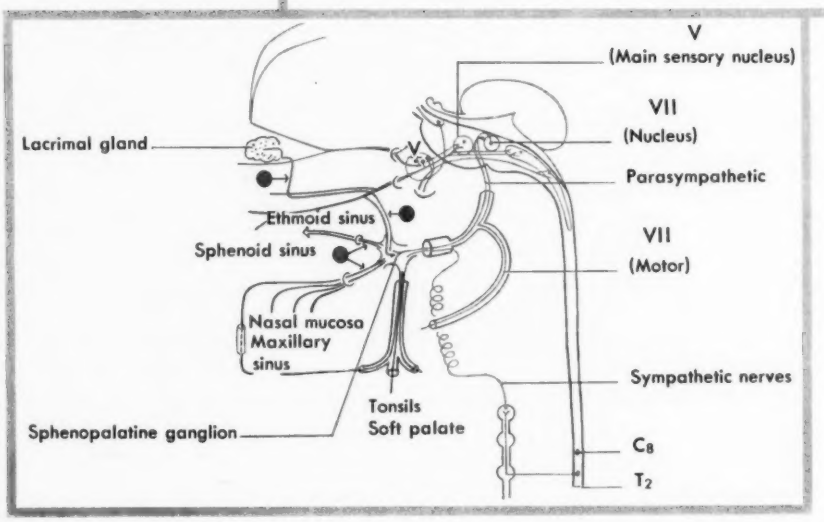
Secretory and vasodilator fibers for the glands and mucosa of the nose, soft palate, tonsils, uvula, roof of mouth, upper lip, gums, and upper part of the pharynx are carried by fibers from the greater superficial petrosal nerve via the sphenopalatine ganglion.

Secretory fibers for the lacrimal gland are carried by the greater superficial petrosal nerve to the sphenopalatine ganglion, thence via the zygomatic nerve and lacrimal branch of the ophthalmic division of the trigeminal.

Vasoconstrictor fibers are carried by the sympathetic fibers from the carotid plexus via the deep petrosal nerve to the sphenopalatine ganglion.

Sensory supply to the sphenopalatine ganglion is carried by two branches of the maxillary nerve.

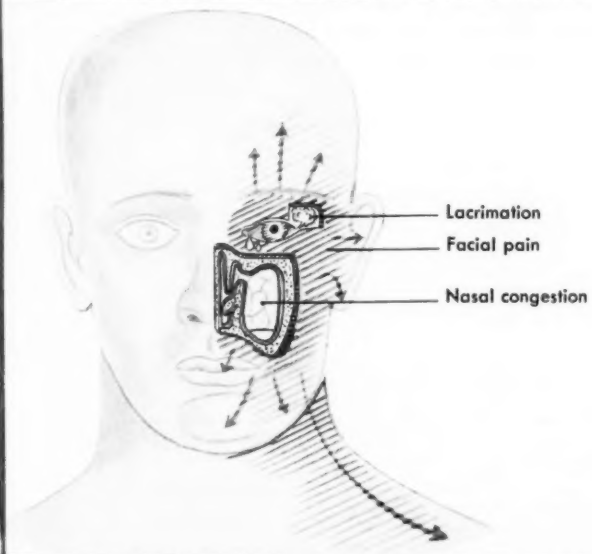




Classification of Atypical Neuralgias

Considerable confusion has existed regarding the nomenclature of this group due to lack of understanding of its mechanism. Frazier and Russell (1924) suggested the term atypical neuralgia. Before and since that time, close variations of atypical facial and head pain have been described under a variety of names. Present opinion is that the underlying pain mechanism is neurovascular and that the clinical syndrome is related to migraine.

Red migraine	Mollendorff, 1867
Sphenopalatine neuralgia	Sluder, 1908
Erythromelalgia of the head	Bing, 1910
Sympathetic hemicrania	Pasteur Vallery-Radot, 1925
Migrainous (ciliary) neuralgia	Harris, 1926
Carotidynia	Fay, 1932
Vidian neuralgia	Vail, 1932
Autonomic facial cephalalgia	Riley, 1935
Histamine cephalalgia	Horton, 1941
Petrosal neuralgia	Gardner, 1947

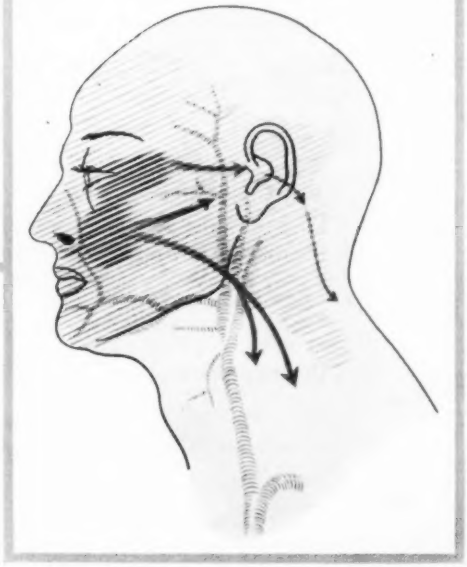


Temporomandibular joint syndrome, Costen, 1934

Pain referred to face or head; burning throat, tongue, side of nose; salivation; deafness and dizziness.

Signs and Symptoms

Pain Distribution



Treatment—Symptomatic

Pharmacotherapy, Specific

MEDICATION	ACTION
CAFERGOT®	
Ergotamine tartrate plus caffeine	Vasoconstrictor
CAFERGOT P-B®	
Ergotamine tartrate plus caffeine	Vasoconstrictor
1-Belladonna	Antispasmodic
Pentobarbital sodium	Sedative
WIGRAINE®	
Ergotamine tartrate plus caffeine	Vasoconstrictor
Belladonna alkaloids	Antispasmodic
Acetophenetidin	Analgesic
MIGRAL®	
Ergotamine tartrate plus caffeine	Vasoconstrictor
Belladonna alkaloids	Antispasmodic
Cyclizine hydrochloride	Antiemetic

(All the above are available in tablet and suppository forms.)

Pharmacotherapy, Nonspecific

MEDICATION	ACTION
EMPIRIN® Compound	
Acetylsalicylic acid	Analgesic
Acetophenetidin and caffeine	Sedative
AMYTAL®	
Amobarbital sodium	Sedative
SINUTAB®	
N-acetyl-para-aminophenol	
Acetophenetidin	Analgesic
Phenyltoloxamine dihydrogen citrate	Tranquilizer
Phenylpropanolamine hydrochloride	Vasoconstrictor
CODEINE PHOSPHATE	Analgesic
DARVON®	
Dextro propoxyphene	Analgesic

(All the above are available in tablet form.)

reatment—Prophylactic

1. General measures

Avoidance of fatigue and stress.
Adequate hygiene.
Avoidance of specific activities which may precipitate an attack (dietary indiscretions, alcohol, etc.).
Elimination of offending allergens; correction of any metabolic defects (rarely significant).

2. Pharmacotherapy

MEDICATION	ACTION
AMYTAL®	
Amobarbital sodium	Sedative
BELLADENAL®	
l-Belladonna	Antispasmodic
Phenobarbital	Sedative
CHLOR-TRIMETON®	
Chlorprophenpyridamine	Antihistamine
DILANTIN®	
Diphenylhydantoin	Anticonvulsant
MILTOWN®, EQUANIL®	
Meprobamate	Tranquilizer
ULTRAN®	
2-p-Chlorophenyl-3-methyl-2, 3-butanediol	Tranquilizer

3. Psychotherapy

Attempt to give patients understanding and insight into their life situations.
Re-education and reorientation with respect to the patient's personal, economic and social life.

4. Surgery

In general, these procedures should be avoided.

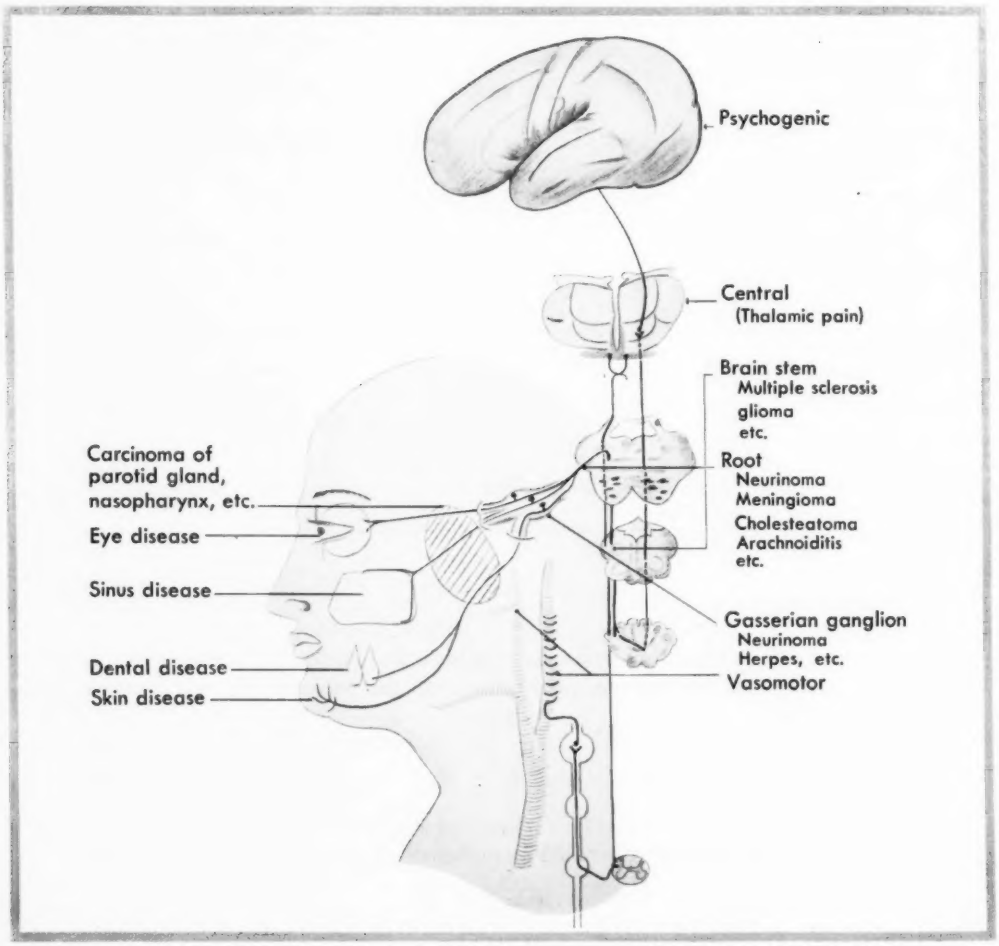
Facial Pain Due to Other Causes

Classification: Facial pain secondary to extracranial and intracranial causes

Pain in the face is carried by specific neuroanatomic pathways. Disease entities may affect these pain pathways at one or more levels, and may be considered as involving the following mechanisms and sites.

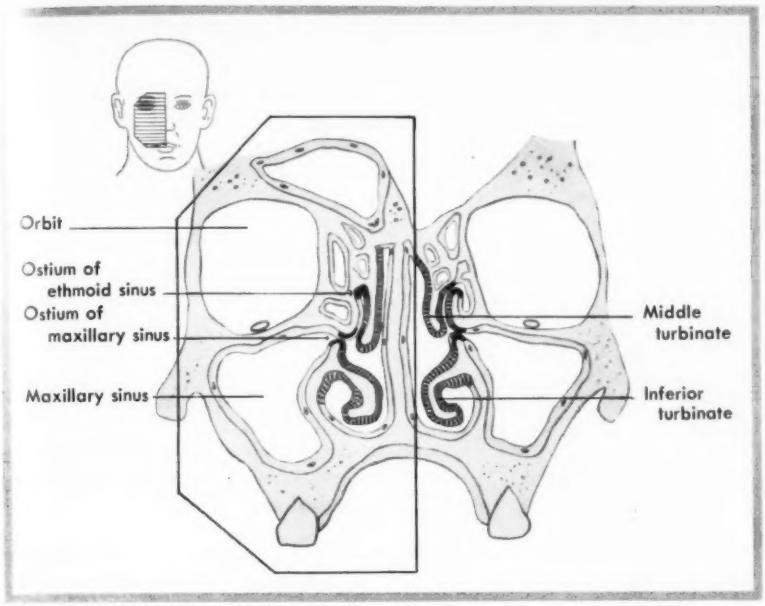
1. Cerebral (psychogenic)
2. Central (thalamic pain, brain stem, spinal cord)
3. Posterior root
4. Ganglion
5. Peripheral nerve and specific nerve endings for pain
6. Vascular

Such a classification has many defects but allows a rational approach to diagnosis and therapy.



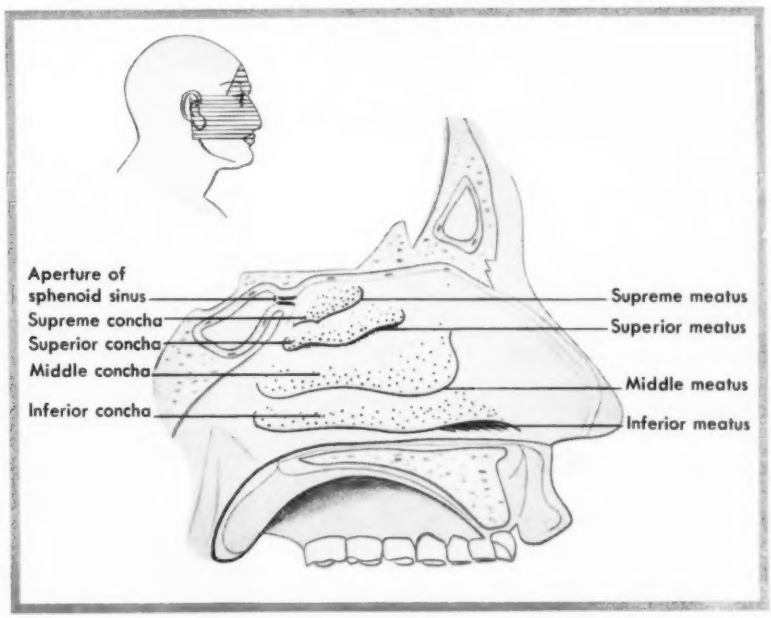
Pain pathways

natomy of Nose and Paranasal Structures, Lateral and Medial Views



Normal anteroposterior

Mucosa covering the approaches (ostiums) to the paranasal sinuses as well as the turbinates are the most pain-sensitive of the nasal and paranasal structures.



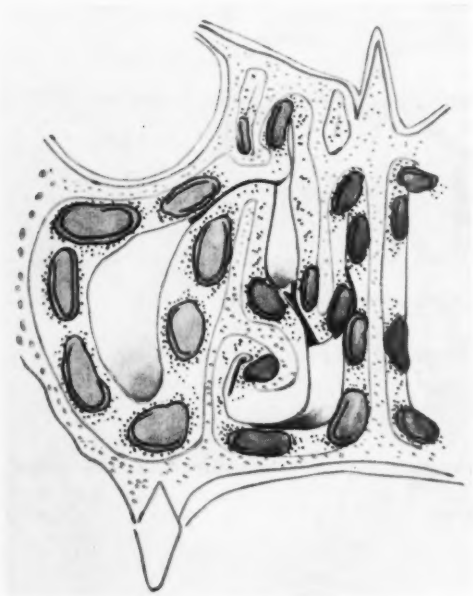
Normal lateral

Stimulation of nasal mucosa results in sustained deep, aching, non-pulsatile pain, associated with lacrimation, photophobia, erythema and hyperalgesia. Pain is referred mainly to the second division of the fifth cranial nerve.

Pathology of Nasal and Paranasal Structures

Sinusitis (Acute)

The pain and headache which occur are due to inflammatory changes in the mucosa of the ostium of the sinus, accompanied by engorgement of the turbinates with impingement on the septum.



Symptoms

Pain is frequently constant, dull, aching, severe, either unilateral or bilateral, referable to region of infected sinus.

Frontal—Forehead

Maxillary—Cheek

Sphenoid—Deep and behind eyes

Ethmoid—Pain around eyes, bridge of nose

Pain is increased in severity by straining, coughing, and changes in posture.

Signs

Inflamed nasal mucosa

Nasal engorgement, edema

Purulent discharge

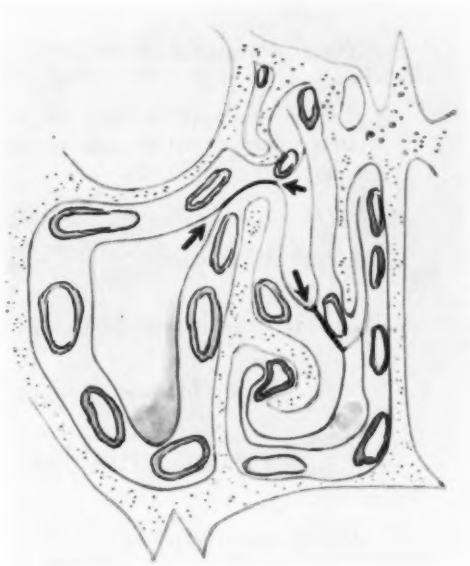
Tenderness to pressure

Temperature elevation

Positive x-ray findings

Vasomotor Rhinitis

Pressure of edematous membranes leads to closure of openings of paranasal sinuses; there may be associated nasal polyps.



Symptoms

Pain may be dull, pressing, occasionally throbbing, varying in severity, usually frontal or temporal. Vasomotor rhinitis commonly is associated with clinical manifestations of sinusitis and nasal polyps.

A family history of allergy and other allergic manifestations often is elicited.

Signs

Obstruction of nose and nares

Paroxysmal sneezing

Swollen mucosa, gray to red

Serous discharge

Treatment

In all these conditions, management of the underlying disorder is the primary goal of therapy. Careful psychologic study of the patient should be made prior to administration of a habituating drug or the use of nerve blocks and other surgical procedures.

Nasal, Paranasal Disorders

Treatment should be conservative and directed toward eradication of the infection, improvement of sinus ventilation and drainage, and removal of offending allergens.

General Measures

Rest, avoidance of fatigue.

Adequate hygiene.

Shrinkage and suction.

Pharmacotherapy

MEDICATION	ACTION
Sinutab	
N-acetyl-para-aminophenol	
Acetophenetidin	Analgesic
Phenyltoloxamine dihydrogen citrate	Tranquilizer
Phenylpropanolamine hydrochloride	Vasoconstrictor
Penicillin	Antibiotic
Chlor-Trimeton	
Chlorprophenpyridamine	Antihistamine

Surgery

Correct any septal deformity.

Remove nasal polyps.

EXAMPLE OF THERAPY FOR A SPECIFIC DISORDER

Facial Pain Secondary to Inoperable Carcinoma of the Parotid Gland

In an attempt to relieve such pain, surgical section (by way of a posterior fossa approach) of the sensory root of the fifth nerve, the ninth nerve and upper vagus (tenth) rootlets, and the posterior roots of C2 and possibly C3 may be required. Occasionally, section of the nervus intermedius also must be added.

When the pain is not amenable to a single surgical approach, lobotomy may be required. Drug therapy (narcotics) would seem justified in a similar situation with shorter prognosis.

Psychogenic Pain

Psychogenic pain cannot be distinguished from pain of physical origin; both are "real." Most pain has a physiologic basis, but neurotic mechanisms exaggerate the suffering.

Description

More common in women.

Excessively dramatic, vivid, primitive.

Location and character change and vary with direct questioning and on suggestion.

Severity of pain varies with individual; no criteria.

History

Onset—Initial pain may have occurred at the time of a significant event in the emotional life of the patient, which occasionally may be associated with a painful lesion of the face.

Further emotional upset may lead to recurrence of painful response without an organic lesion.

Physical examination—Reveals no physical cause for pain.

Response to drugs.

Real pain and "imaginary" pain can be relieved by hypnosis, suggestion, placebo and distraction.

Patients with certain types of psychologic difficulties become dependent on analgesics more quickly.

Character structure—Masochistic.

Dynamics

1. Repressed hostility—rage—for which punishment is deserved.
2. Forbidden instinctive impulses—punishment for attempts to gratify such impulses.

CLINICOPATHOLOGIC CONFERENCE

Report From Veterans Administration Hospital, Hines, Illinois

Edited by William J. Gillesby, M.D., Assistant Chief, Surgical Service

Case Report

A 62 year old white man was first admitted to Hines Veterans Administration Hospital on February 15, 1956. He gave a history of frequency and nocturia of one year's duration, and he had had hematuria with bright red blood for the preceding four months.

Physical examination on admission revealed that the patient was well developed but thin. Auscultation of the lungs showed inconstant dry rales at the right base. A grade 2 systolic murmur in the pulmonary area was noted on examination of the heart. No tumor masses were palpable in the abdomen, and on deep inspiration the liver border was palpable one fingerbreadth below the costal margin. The prostate was 1 plus enlarged, smooth and symmetric.

Laboratory tests on February 15 included three cultures and three smears of the urine for acid-fast bacilli. The results of all these tests were negative. One urine culture revealed the presence of hemolytic *Staphylococcus pyogenes* var. *albus*, coagulase negative.

On February 17, a cystoscopic examination showed contracture of the bladder neck, a diverticulum of the left side of the bladder wall, and a fungating tumor mass on the right side of the bladder. In a chest x-ray on the day following admission, a fine, diffuse nodularity was seen and the lung fields appeared hazy. The cause of this condition was undetermined; however, sarcoidosis was considered as a possible diagnosis.

On February 21, the bladder neck was resected and 4 gm. of tissue was removed. The bladder tumor also was resected and the area was thoroughly fulgerized. Pathologic examination of the tissue revealed a grade 3 transitional-cell carcinoma of the bladder. The patient's immediate postoperative course was uneventful until March 1, when he began to have difficulty in voiding. On March 7, an additional 4 gm. of residual prostatic tissue was removed surgically. The pathologic report of a biopsy of the area of the previous tumor showed inflammation, but no recurrence of tumor was noted.

The patient was discharged on April 18. The final diagnosis was grade 3 transitional-cell carcinoma of the urinary bladder and the presence of nodular pulmonary lesions, probably due to sarcoidosis. Operation for the carcinoma had resulted in improvement; the lesions of the lung had not been treated and remained unchanged at the time of discharge.

When the patient was rechecked six weeks after having been discharged, a papilloma of the posterior bladder floor on the right side

was noted and fulgerized. Cystoscopic examination on December 21 revealed a second recurrence of the tumor in the same area, and fulguration was again performed. The tumor had not recurred when the patient was reexamined on April 19, 1957.

The patient was readmitted to Hines on June 19, 1957, complaining of a cough of three weeks' duration. The cough had produced small amounts of gray-white sputum, and, two weeks before admission, small amounts of blood were noted in the sputum. The patient had lost 5 lb. in the preceding three weeks. There had been no recurrence of bladder symptoms since his last checkup, and he did not appear to be ill. The lungs were resonant to percussion throughout. Median coarse inspiratory rales were heard in a few isolated areas of the chest, and bronchovesicular breath sounds were heard over most of the chest. The abdomen was scaphoid and no masses were palpable. Blood pressure was 120/80. Additional history elicited at this time revealed that the patient had worked for two years during the 1930s at a cement plant, where he had emptied cement out of bags.

The patient was given a course of 600,000 units of penicillin twice a day for one week; however, no response was noted. He was afebrile on admission and continued to be so. A chest x-ray on June 19 showed a patchy homogeneous infiltrate in the right middle and upper lobes and in the left midlung field. More opaque densities were noted in the left middle and lower lung fields. A recheck on July 5 showed no change. These findings were interpreted as indicating possible metastatic disease, pulmonary adenomatosis and fungous infection.

On June 21, laboratory tests showed that the erythrocyte sedimentation rate was 10 mm. per hour. Urinalysis revealed a specific gravity of 1.005, albumin 2 plus, and no sugar. There were seven to nine white blood cells and 10 to 12 red blood cells per high-power field. Numerous bacteria were seen. Three sputum cultures and three sputum smears were negative for acid-fast bacilli, and six sputum cultures were negative for fungi. Results of a smear and culture of tracheobronchial secretions for acid-fast bacilli also were negative. A sputum culture on July 18 revealed the presence of *Neisseria catarrhalis, Pneumococcus* and alpha *Streptococcus. N. catarrhalis* and hemolytic alpha *Streptococcus* also were observed in a sputum culture on July 23.

A chest x-ray on July 29 showed no change. Skin tests were positive to first-strength purified protein derivative and histoplasmin. The results of an electrocardiogram were within normal limits. On July 16, a bronchoscopic examination gave normal findings. In a bronchogram on July 30, the right apical and posterior segments were not visualized. There was moderate visualization of the basal bronchus on the left side. No bronchiectasis was observed. A cystoscopic examination revealed no recurrence of the original tumor in the bladder.

On August 8, weakness of the right side of the mouth suddenly developed and the patient became mute. In two weeks he regained partial control, but on September 1 weakness of the entire right side of the body and aphasia developed. Anticoagulants were started and the diagnostic workup was postponed indefinitely. A progress note on September 7 stated that the patient had had three episodes of hemoptysis that day, presumably from nasal hemorrhage due to septal ulcerations. Examination of the chest at this time revealed harsh rales over the right lung. For the first time during this hospitalization, the patient had a fever, which rose to 105° F. at midnight. The patient was found dead in bed on September 8, 1957.

Discussion

DR. EDWARD J. BEATTIE (attending physician, thoracic surgery): This patient was admitted to the hospital because of a urinary ailment. Physical examination on admission was not particularly remarkable. Although he had a systolic heart murmur, there were no other stigmas of cardiac disease. The patient seemed to have many obstructive symptoms; however, the enlargement of the prostate did not seem to be of sufficient degree to be typical prostatism. This seemed to be a median bar-type enlargement without the diffuse enlargement of the gland. A malignancy of the urinary tract

might have been suspected, but blood in the urine per se is more commonly associated with benign hypertrophy of the prostate than with a malignancy.

The contracture of the bladder neck revealed at cystoscopy must have been due to the prostate gland, because after each of the two operations for removal of prostatic tissue the obstruction was relieved. I do not think that the diverticulum of the left side of the bladder wall was responsible for the urinary retention. The fungating tumor mass on the right side of the bladder, which was diagnosed as a malignancy, could very well have caused the blood in the urine.

The chest x-ray made in February 1956 showed a pathologic condition in the lungs; however, from the description of the findings, this condition did not seem to be due to the tumor in the bladder. I have observed that bladder tumors commonly do not metastasize to the lungs; this occurs more often with tumors of the kidneys.

Sarcoidosis also was considered as a possible diagnosis in this patient. To confirm a diagnosis of sarcoidosis, I think it is valuable to use the standard medical methods first, including a skin test, sputum examination and culture, guinea pig inoculation and cultures for tuberculosis. These steps should be followed by bronchoscopy. The next logical procedure in examination for suspected sarcoidosis is a scalene node biopsy. In my experience, scalene node biopsies have given about 80 per cent positive results in sarcoidosis. If the scalene nodes are negative, a lung biopsy may establish the diagnosis. I think that surgeons can be very helpful to physicians by removing tissue for biopsy and seeing that it is studied both bacteriologically and pathologically.

The patient was readmitted to Hines after having been reasonably well for approximately 16 months. At this time, he complained of a cough productive of gray-white sputum. In itself, this is not indicative of an ordinary bacterial infection; in the presence of such an infection, the sputum is yellowish or greenish. The small amounts of blood noted in the sputum two weeks prior to admission could not be considered a specific symptom, since persons with colds frequently spit up small amounts of blood when they cough hard. This is particularly true when the humidity in the house is low, as during the winter months.

The patient had had no recurrence of bladder symptoms since his last hospitalization. Thus, it was necessary first to determine whether his present illness was a new disease or was related to the carcinoma of the bladder. The physicians who were taking care of him obviously suspected some kind of infection, since penicillin was prescribed for one week. The fact that the patient was afebrile on admission and continued to have no fever was contrary to the course of most infections; an infection involving both lungs ordinarily produces some degree of fever.

Over a period of six weeks, there was no progression in this patient's condition. Skin tests were positive to tuberculin and histoplasmin. It was not specifically mentioned, but I would imagine that the possibility of blastomycosis and coccidioidomycosis had been considered. Blastomycosis can simulate tuberculosis; with a positive skin test, the physician searches more diligently for blastomycetes in making a diagnosis. An underlying bronchiectasis evidently was considered, since a bronchogram was done; however, with the exception of nonvisualization of the right apical and posterior segments, the bronchogram did not give a particularly abnormal picture.

At this point, this patient had cancer of the bladder and an undiagnosed pulmonary lesion which either had progressed or had recently occurred. In August 1957, however, a third condition developed. The patient had a sudden weakness on the right side of the face and mouth. Men of this age are heir to other diseases and the so-called stroke; however, I think that the medical department always should explain the reason for a stroke in persons who otherwise are in good physical condition. Many strokes are caused by tumors or aneurysms, and some are just a result of occlusion of the carotid or vertebral arteries. I do not think that you can disregard strokes, saying that they are just acts of God, and quibble about whether or not to use anticoagulant therapy.

This patient recovered to some extent from the mild stroke; however, three weeks later, hemiplegia occurred on the right side. Treatment should have been initiated after the mild stroke; however, anticoagulants were started after the development of hemiplegia. According to the laboratory report of 14.2 and 22 per cent prothrombin, the patient reached reasonable levels of control. He apparently was given a prothrombin depressant, which started a hemoptysis thought to be due to the nose. Any person with a history of hemoptysis who receives anticoagulants may be headed for trouble. Harsh rales were heard over the right lung; a fever of 105° F. developed, and the patient subsequently died.

Frequently, people who have strokes drown in their own juices. They aspirate and they do not swallow well; they present feeding problems and they do not cough. Pneumonia is one of the most common causes of death in a person who has hemiplegia.

No x-rays were made of this patient at this time. Death could have been caused by a progression of the pulmonary disease; however, this really does not seem likely, as the pulmonary lesion had not changed over a period of six weeks. It seems that death more probably was due to an acute event secondary to the hemiplegia.

The laboratory work in this case was not helpful to me. The urinary findings would be expected in the presence of obstruction and bleeding; however, the nonprotein nitrogen was normal and the patient's kidney function apparently was all right. Bleeding, coagulation and prothrombin times were normal until anticoagulants were administered. Results from repeated sputum cultures were negative. The sedimentation rate of only 10 mm. on June 21, 1957, was remarkably low if this man had an infection. The protein levels stayed normal and the globulin went as high as 3.3 with an albumin of 3.4. Globulins do go up in sarcoidosis and some other diseases. It also is interesting that this patient at no time had any eosinophilia, because parasites sometimes can cause diffuse patchy infiltrations.

DR. WILLIAM FREDERICK (assistant chief, radiology service): An x-ray on February 16, 1956, showed a somewhat irregular density throughout, with some pleural thickening at the right costophrenic and cardiophrenic angles. An x-ray dated about 16 months later showed extensive irregular density throughout both lung fields, primarily in the upper third on the right side and in the lower half of the right side of the chest, which was fairly sharply limited by the short fissure. The density was considered semihomogeneous. Drainage bands were suggested from the upper right side of the chest leading to the hilus.

Differential diagnosis from these findings would include a vast number of diseases. An inflammatory process might well have been the first possibility considered. A bronchogenic carcinoma is always a possibility, and, in view of the history, a metastatic malignancy was a strong possibility in this case. The x-ray appearance, however, was not typical of the usual metastatic malignancy. On the other hand, nothing is perfectly typical of any metastatic malignancy.

To summarize, the findings in this patient were not really typical of any condition. Although the x-ray appearance suggested a malignancy, it could not be determined whether it was primary or secondary. The length of the illness tends to make the possibility of a malignancy less likely. It seems more probable that this patient had a type of chronic inflammatory process. I neglected to mention the possibility of alveolar (cell) carcinoma. The findings in the chest could have indicated such an entity. The appearance did suggest a pulmonary adenomatosis; however, there was really no pathognomonic condition observed in the series of chest x-rays.

DR. BEATTIE: I agree with you. Although the findings in this case did not seem to be entirely typical of any one disease, I would like just to comment on a few things.

If you did not know this patient's history and if you observed only one particular chest film, you would think right away of an aspiration pneumonia. The picture was the same as that observed when a patient has been vomiting blood.

Emboli also can give very peculiar looking chest x-rays. The patient apparently had no

fibrillation. There were no emboli in the veins, although the possible stroke could have indicated an embolus in the head. Fat emboli also can produce unusual symptoms, but this patient had had no fractures or condition which would result in fat emboli. The possibility of pneumonitis was ruled out by the findings at x-ray examination.

We must consider the possibility of a fungous infection. Assuming that results of skin tests other than those given in the laboratory data were negative, certain fungous infections may be ruled out. However, in trying to relate cerebral symptoms to unknown conditions in the chest, the possibility of an infection with *Toxoplasma* must be considered. Infection with this organism can produce symptoms in the lungs with cerebral manifestations. Collagen disease also can give pleural effusions, changes in the lungs, fibrosis, and unusual pneumonitis; however, there were no other symptoms in this patient compatible with a diagnosis of collagen disease. There was nothing in the laboratory protocol to indicate that the tests for lupus erythematosus were performed; therefore, this disease probably was not considered.

Thus, we come back to the possibility that this patient had a tumorous condition in the lung. Both primary and metastatic tumors must always be considered in patients who have lung symptoms. This patient could have had a metastatic tumor from an unsuspected primary source in addition to the primary tumor in the bladder. Metastases from bladder tumors must occur; however, I have not seen any. I believe that most tumors in the bladder spread locally before they get into the blood stream; however, tumors from the kidneys frequently spread to the lung.

It is possible to cure patients with metastatic lung disease. The first known cure, although I use the term advisedly, was in a patient of Dr. Churchill's at the Massachusetts General Hospital. The patient had a hypernephroma, which was treated by a nephrectomy, and a metastasis to the right middle lobe, which was treated by a middle lobe lobectomy. The patient was alive and well 20 years later. At Presbyterian Hospital, we have treated metastatic lung tumors very aggressively, having operated on about 30 patients in the last few years. Several of these patients are alive and well at the present time.

The condition in this patient was diffuse and bilateral, so it did not appear to be a malignancy which could be treated surgically. It did not look like the typical metastatic malignancy; they usually are more solid, discrete patches, but then metastatic malignancy can present almost any kind of a picture. I think a bronchogenic primary tumor and pulmonary adenomatosis should be considered. You can never rule out the possibility of a primary bronchogenic tumor. Usually, there is more hemoptysis in pulmonary adenomatosis than this man had, and this condition is more common in women than in men, as well as being more frequently seen in younger people. The disease process in pulmonary adenomatosis is usually of longer duration than that in this patient. Another indication of pulmonary adenomatosis is a tenacious mucoid sputum, and such was not described in this patient.

Considering the amount of lung disease in this patient, it is interesting that there was not more hilar adenopathy. This is not consistent with a diagnosis of sarcoidosis or, to a certain extent, of bronchogenic carcinoma. Thus, my first diagnosis would be a fungous infection due to an organism such as *Toxoplasma;* my second consideration would be a peculiar variety of tumor, possibly metastatic but probably not from the tumor in the bladder.

DR. ALICE DAKIN (resident in pathology): In answer to one of your questions, only those skin tests mentioned in the laboratory data were performed.

DR. FREDERICK: The roentgenographic picture in this case suggests a mixed metastatic malignancy. If it actually was a metastasis, it could have been nodular and lymphatic. Hodgkin's disease will sometimes present a similar picture. I have tried to determine how one can diagnose a primary disease from the secondary metastatic findings in the chest, but I have not been successful. Some authors mention the typical appearance of metastases; however, in practice, there seems to be little validity in their criteria for identifying a primary malignancy from the metastatic picture.

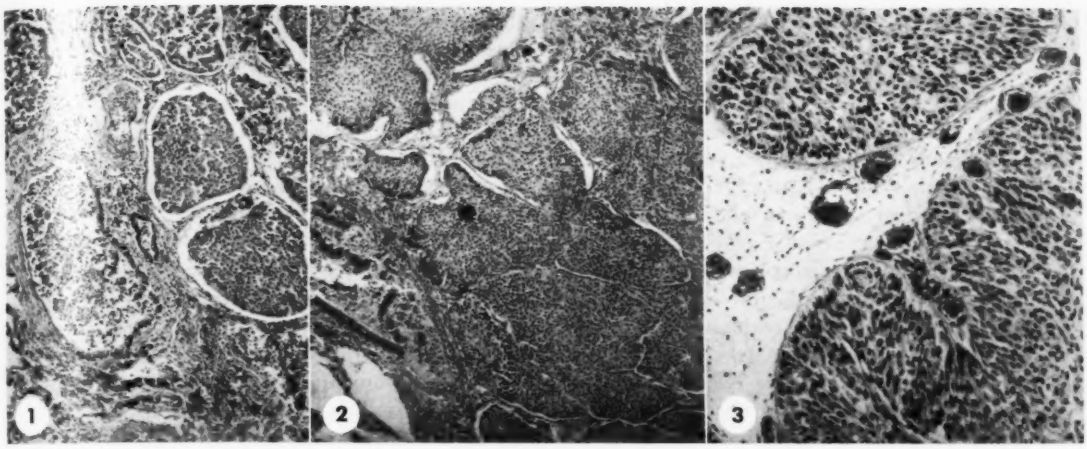


FIGURE 1. Metastatic tumor in the bronchiole and in the vessels of the lung.

FIGURE 2. Metastatic tumor (transitional-cell carcinoma) present in the lung.

FIGURE 3. Original tumor (transitional-cell carcinoma) that was removed from the bladder.

DR. DAKIN: Autopsy revealed a carcinoma in the right upper bronchus and right upper lobe, with metastases in both lungs and regional lymph nodes. Microscopic examination showed that this was a transitional-cell carcinoma, metastatic from the urinary bladder. In addition, bronchopneumonia was present in both lower lobes. The patient also had a mild silicosis, which was demonstrated with polarizing light in the regional lymph nodes. Examination also showed fibrous pleurisy over the right lung, fatty metamorphosis of the liver with chronic passive congestion, accessory spleen, diverticula of the urinary bladder, and scarring of the bladder mucosa where the tumor had been removed. There was no evidence of tumor on gross examination.

Figure 1 shows a nest of tumor cells in one of the bronchioles. Some tumor cells also are seen in a vascular channel. Figure 2 shows detail of the tumor cells in the lung which is characteristic of transitional-cell carcinoma. There are fine connective tissue tendrils between the layers of cells. The oval nuclei of the tumor cells in the muscularis mucosae of the bladder are seen in figure 3. These cells are fairly deep-staining. The pale cytoplasm is vacuolated in places, and the cell borders are indistinct. This definitely suggests transitional epithelium similar to that seen in the lung.

Transitional-cell carcinoma of the bladder is papillary in structure in 80 to 90 per cent of cases. It is apt to represent a fairly low percentage of all malignancies, varying from 1 to 3 per cent, and the incidence of this type of carcinoma in men and women is three to one. It usually occurs between the ages of 55 and 70, and seldom is seen in patients less than 45 years old.

The tumor in this patient was classified histologically as grade 3. Grade 1 transitional-cell carcinoma is a benign-appearing tumor with normal transitional cells. No invasion is seen anywhere and there is no nuclear variation. Normal mitoses are occasionally observed and papillary configuration is seen. In grade 2, there is some beginning pleomorphism and anaplasia of the cells. There may be some invasion or infiltration in the tunica propria mucosae and some gross changes in the papillary structures, with widening and some fusion of the villi. Mitotic figures frequently are seen. In grade 3 transitional-cell carcinoma, there is always invasion of the muscularis mucosa of the bladder wall and there is much more anaplasia and pleomorphism than in grade 2. There is so much anaplasia and invasion of the tumor in grade 4 transitional-cell carci-

noma that it is difficult to identify the cells as transitional.

Some authorities say that only 8 per cent of all bladder carcinomas metastasize; others quote figures as high as 56 per cent. One of the primary methods of spread is by contiguity and invasion through the bladder wall into the perivesical structures and then into the rectum, sigmoid, broad ligament, uterus, vagina and adjacent structures. The metastatic routes are either lymphatic or through the vascular channels. The regional lymph nodes are involved in approximately 60 per cent of the metastatic lesions, the liver in about 50 per cent, and the lungs in about 35 per cent. These tumors do metastasize to bone, but not as often as do some other tumors. If they have extended into the prostate, their metastatic route is apt to be that of a primary tumor of the prostate, occurring in bone or in the lungs. The degree of histologic malignancy in these cases has some bearing on the percentage of metastases, in that the tumors that are very superficial (grade 1 transitional-cell carcinoma of the bladder) are much less apt to be metastatic than are those that show invasion of the tunica propria mucosae, penetration into the muscularis mucosae, or deep infiltration into tissues surrounding the bladder. If there is a metastatic lesion in the lung, it, too, can spread throughout the lung by the same route by which a primary carcinoma spreads; thus, it is difficult to differentiate between the two. When multiple lesions are seen on x-ray, it is necessary to prove that it is not metastases rather than a primary tumor.

The neuropathologist did not find, either grossly or microscopically, any pathologic condition in the brain of this patient. The carotid arteries showed minimal arteriosclerotic changes. The remaining prostatic tissue showed no changes, and there were no metastatic lesions. Only scarring was observed.

DR. MYRON E. RUBNITZ (chief of pathology): The pathologists who reviewed this case thought that they saw something grossly which resembled bronchogenic carcinoma. Metastatic lesions may erode into a bronchus, so it is sometimes difficult to state whether a metastatic or primary lesion is present in the lung. The fact that there was bronchial involvement does not necessarily mean that this was a primary carcinoma.

What was the cause of this patient's death? I would assume that it was just an overwhelming pneumonia with pulmonary metastases.

Postgraduate Clinical NOTES

144. DISCOGENIC DISEASE

Aging leads to chemical change in the nucleus pulposus of the intervertebral disc, and thus causes mechanical deficiency. When, under stress, degeneration of the disc becomes more rapid than the repair process, pain (backache) is produced. Discogenic disease may result in rupture, osteoarthritis or healing. Healing may be achieved by proper rest, exercise, nutrition and hormonal therapy. Relative ischemia in muscles and other structures may contribute to the metabolic failure; this condition is aggravated by lack of exercise. Another factor is stagnation hypoxia due to venous stasis, which may occur during prolonged immobilization.

S. Vernon, Discogenic disease, backache and connective tissue function, *Journal of the American Geriatrics Society*, March 1960, pp. 195-199

Protein Economy in the Growing Child

L. EMMETT HOLT, JR.*

New York University College of Medicine, New York

L. EMMETT HOLT, JR.

THE idea that "we are what we eat" goes back to ancient times. Some of us will recall from our school days Dido's outburst at the perfidy of Aeneas, charging that he must have been nursed by Hyrcanian tigers to have been imbued with such cruelty. The idea crops up again and again in history, and there are suggestions of it even in recent times. Not long after World War I Orr and Gilks[1] reported on the attributes of two East African tribes who lived in juxtaposition—the Masai and the Kikuyu. The Masai were fond of meat, milk and blood puddings. They were vigorous, aggressive and warlike in contrast to their gentler vegetarian neighbors, the Kikuyu. In more recent times, however, the dietary habits of these tribes are said to have changed. The once placid Kikuyus have learned to eat and like animal protein, and it seems it was they who were responsible for the Mau Mau rebellion.

Be that as it may, the concept that mental traits are determined by diet is not accepted today. We recognize that frank malnutrition may lead to apathy, but we are not inclined to attribute the differences between Hitler and Nehru to the diets of their formative years. Physical status is, however, a different matter. Although we realize that a wide variety of diets is compatible with apparent health, the range between undernutrition and overnutrition for most nutrients being a wide one, it has also become clear that some differences in body composition and in body function do occur between these extremes. Being perfectionists, "the optimum diet" has a great appeal for us. We want optimum nutrition—that which will give us the greatest measure of health and of well-being—both for ourselves and for our children.

During the last few years there has been considerable interest in protein nutrition, and

*Professor of Pediatrics, New York University College of Medicine, New York, New York.

The Irvine McQuarrie Lecture, delivered in Minneapolis, September 23, 1959.

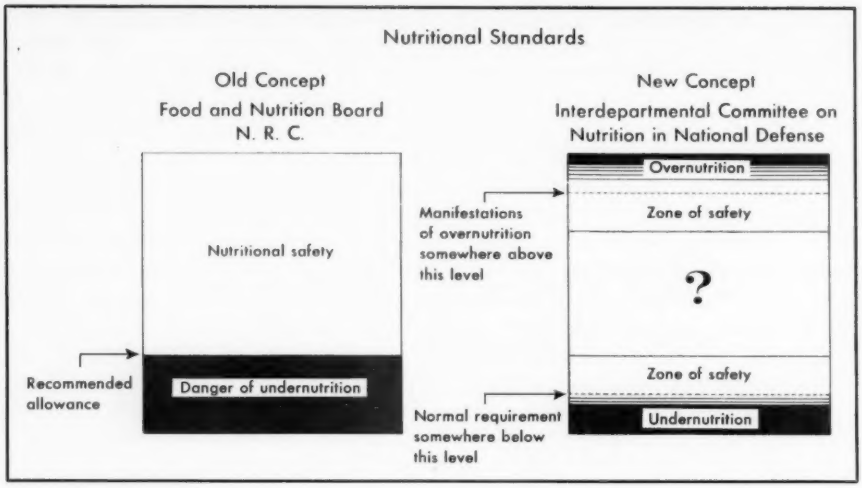


FIGURE 1.

efforts have been made to define optimum intakes of this important foodstuff with somewhat divergent conclusions. Let me say at the start that I am not prepared to give an answer to this problem. At the present time it cannot be given. All I shall attempt to do is to bring together some of the knowledge that has been gained regarding the response of the body to differences in protein intake—responses in body composition and in the resistance to various kinds of stress. Perhaps this will enable us to see a little more clearly the direction in which we should go.

First of all, I want to make clear the aspect of nutrition that I will discuss; it is that area in which there appears to be no immediate danger of either undernutrition or overnutrition, illustrated by the central part of the right-hand section of figure 1.

What happens when we move from a lower to a higher level of protein intake? We have to remember one more qualification; namely, we cannot change one nutritional variable without changing others. If we add or subtract protein from a diet that is constant in other respects, we are adding or subtracting calories; if we are to vary protein and keep calories constant, we must vary other caloric foods (either fat or carbohydrate or both) in an inverse manner. In most of the studies recorded, calories have been kept constant by substituting carbohydrate for protein and vice versa.

TABLE 1

NITROGEN RETENTION OF INFANTS

DIET	FIRST SIX MONTHS* (MG./KG./DAY)	AVERAGE AT TWO MONTHS† (MG./KG./DAY)
Breast milk	121	188
Cow's milk	186	216

*From Swanson.[2]

†From Fomon and May.[3]

Influence of Protein Intake on Body Composition

This subject has interested pediatricians for at least 60 years and has caused a good deal of controversy. Considerable data have been collected which suggest that as the nitrogen intake is increased the body retains more nitrogen. A well-known and often-quoted experiment pointing to this conclusion is that of Swanson,[2] who conducted balance studies on two infants for a six month period. One of the infants was fed breast milk, and the other was fed cow's milk. The nitrogen retention on the latter was far greater, as is shown in table 1.

Similar studies on a group of infants were carried out by Fomon and May[3] in Iowa City. They, too, point to a higher nitrogen retention on the higher intake, a difference which persisted as long as the studies were continued.

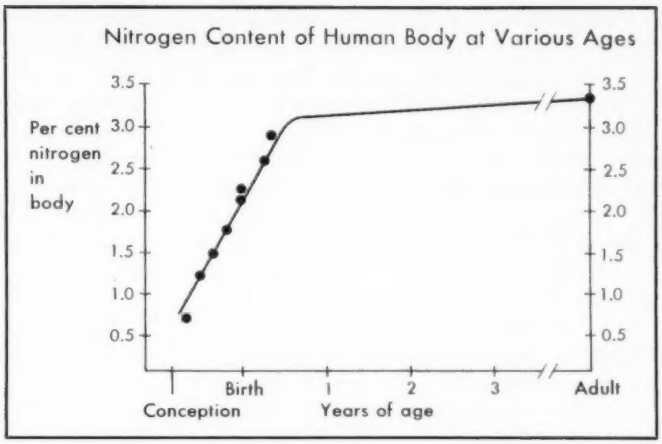


FIGURE 2.
(From Moulton.[5])

This phenomenon has puzzled investigators. Is the body really made more nitrogen-rich by generous nitrogen ingestion, or is there some error in balance experiments? The answer to this question requires direct body analysis. Only a few direct analyses of the growing human body have been made; these have been mostly in deaths resulting from diseases which may have affected body composition. We can, however, get information from experimental animals, since we can analyze the entire body after feeding various diets. The answer seems to be that the apparent gain in nitrogen on the higher protein intake is in part spurious and in part real. Wallace[4] pointed out that in balance studies incomplete collections of food and of excreta do not cancel each other; they produce an additive error. The few drops retained in the feeding bottle will raise the apparent nitrogen intake as the dietary nitrogen is increased, and the incompletely collected excreta, now richer in nitrogen on the high-nitrogen diet, will fail to reveal all of the greater nitrogen loss. Thus, both these errors tend to increase the apparent nitrogen retention on the higher intake. This accounts for the spurious increased nitrogen retention.

That a part of the nitrogen gain appears to be real derives from the fact that the bodies of all animals thus far studied are relatively poor in nitrogen at birth, becoming gradually richer until "chemical maturity" is attained. The rate of chemical maturation varies in different species. In the rat much of it is completed by the time the animal is weaned, the final mature composition being attained at about 40 days. In the calf the process requires several years. The limited data on man, collected by Moulton,[5] indicate that at birth approximately 2 per cent of the body consists of nitrogen. The percentage rises rapidly during the early months. By the age of four months, chemical maturation is virtually complete, the composition now being about 3 per cent nitrogen. A minimal increase occurs beyond this point, but after four years there is no change whatever (figure 2).

It appears that the more chemically immature the body the more readily it can be made to retain nitrogen by a high-protein intake. In premature infants, whose nitrogen content was presumably well below 2 per cent, Snyderman and co-workers[6] observed very large differences in nitrogen retention at different levels of intake, the rate of weight gain being virtually identical. Somewhat similar data were reported earlier by Gordon and associates[7] in experiments of shorter duration. After chemical maturity is attained the nitrogen composition of the body cannot be appreciably altered by diet, as was illustrated in a patient studied by Talbot and co-workers[8] (figure 3). When the nitrogen intake was raised, after a brief period of adjustment the initial retention figure was resumed.

What is the significance of our being able to push more nitrogen into the organism dur-

ing this early period of life? Are we hastening the process of functional maturation, as some like to believe, and thus making the organism better able to withstand the stresses of life, or are we merely pumping in building stones which remain *in situ* until the body is ready and willing to use them? Is the situation similar to that of iron administered during the early weeks which is retained but not incorporated into hemoglobin? This is an important and an unanswered question.

It has seemed to us that some light might be thrown on this problem by investigating the nature of the retained nitrogen at this early age. If it were in the form of protein it would seem that it might well have functional value; if it were in the form of free amino acids its functional value would be more doubtful. A small fraction of the additional retained nitrogen can be accounted for by the increased concentration of nonprotein nitrogen within the extracellular fluids, but the bulk of it must be intracellular. After studying the only readily accessible cells of the baby, red blood cells, Cusworth and co-workers[9] in our clinic made the interesting observation that during the early months of life the concentration of free amino acids is unusually high (figures 4 and 5). Until other cells are studied, one must speak cautiously; however, it appears that at least some of the nitrogen retained in the cells during the period of so-called chemical maturation is in the form of building stones.

Let us turn now to a later period of growth, when the nitrogen composition of the body has reached the mature figure, and see how growth and body composition are affected by altering the nitrogen intake. The rat attains chemical maturity in four to six weeks, and most of the experimental rat studies deal with this later period. It may be seen from the study of Addis and co-workers[10] that growth increases up to a certain point with increasing protein intake, but with further increases it declines (figure 6). The protein composition of the animal remains virtually constant during this same range of intakes, and if fat-free tissue is considered, this constancy of composition is even more striking. Only at extremely low or high levels of nitrogen intake, beyond the range of the study of Addis and associates, can one alter nitrogen composition of the body. Thus Garrow[11] was able to show a marked drop in protein percentage on a protein-free diet, and Halac[12] showed a slight increase (from 18.0 to 19.2 per cent) when the protein of the diet was increased from 27 to 64 per cent.

Despite this constancy in nitrogen composition in the body as a whole, an examination of individual tissues shows that significant alterations occur in the distribution of nitrogen among the different tissues as the nitrogen content of the diet is increased. Certain tissues increase out of proportion to the rest of the body and thus contain a higher proportion of the body nitrogen; other tissues increase only in proportion to the size of the body as a whole, and still others do not share in the growth of the body as a whole and hence contain a smaller proportion of the body nitrogen. The tissues which gain nitrogen out of proportion to the body weight are the kidneys, the liver, the adrenal[13,14] and the spleen. The heart maintains a constant proportion of the total body nitrogen, whereas the brain and organs of special sense fail to increase in size and hence contain a smaller part of the total body nitrogen. *By feeding an animal up on protein you can make his liver grow, but you cannot make his brain grow!* Some of these changes studied by Addis and co-workers[10] in the rat are shown in table 2. Similar changes were observed in pigs by Filer, Baur and Resbeck[15] and are shown in table 3.

Although others had had this idea previously, Walter and Addis[16] clearly formulated the relation between organ size and organ work. On a high-protein diet, the kidney has more work to do, as there is more urea to excrete. The liver has to deaminate more protein, and the adrenal cortex is concerned with gluconeogenesis from surfeit protein.

Some observers have noted a difference between the response of the kidney and that of the liver to a protein work load. The elementary composition of the kidney is little affected by this load; it remains constant as the organ hypertrophies. The liver, on the other hand, tends to increase its nitrogen content as it hypertrophies, as is shown in table 4.

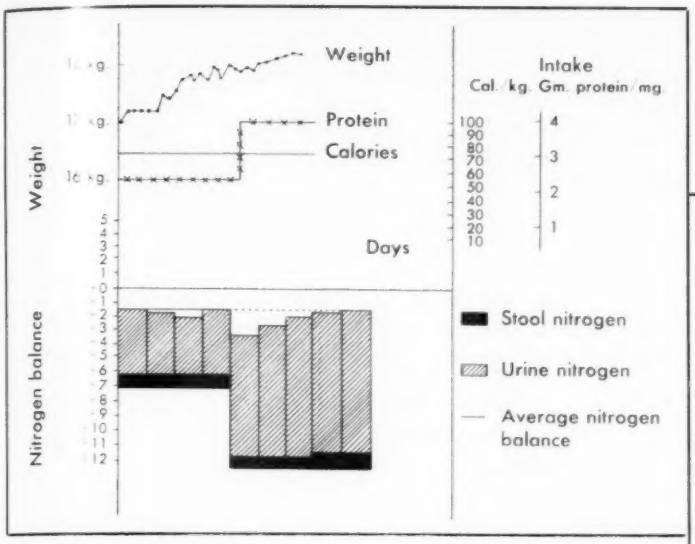


FIGURE 3.
(From Talbot et al.[5])

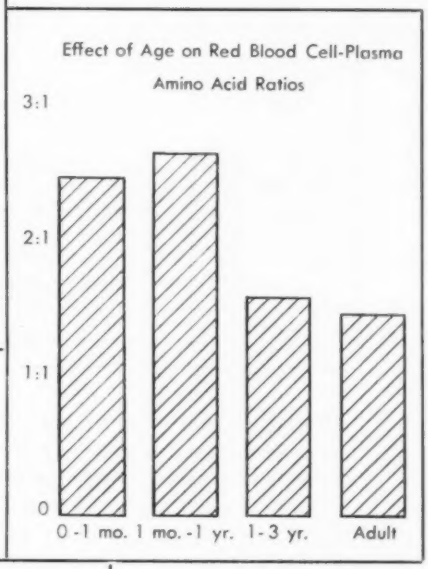


FIGURE 4.
(From Cusworth et al.[6])

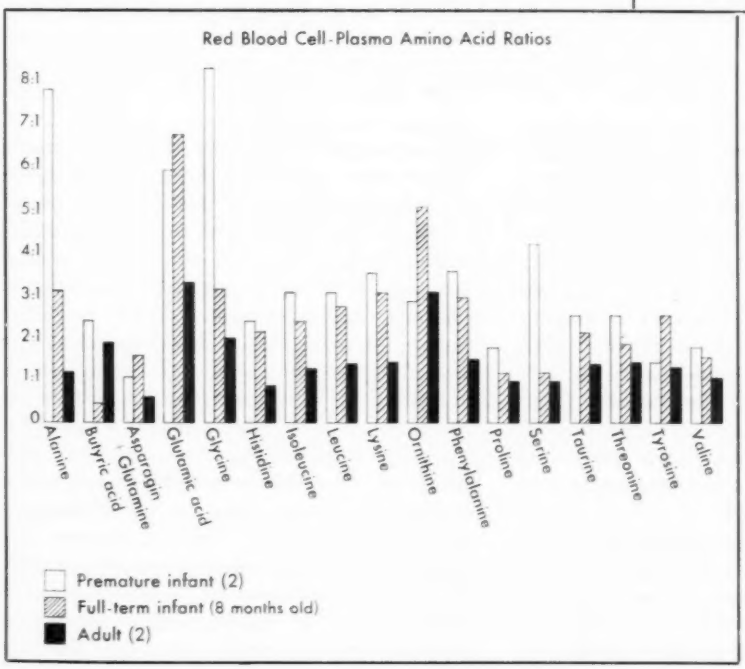


FIGURE 5.
(From Cusworth et al.[6])

Effect of Protein Intake on Body Composition

	Per cent protein in diet				
	6%	11%	16%	27%	43%
Final weight of animal	142.9	160.7	177.0	178.0	165.4
Per cent protein	16.7	16.6	15.5	15.8	16.4

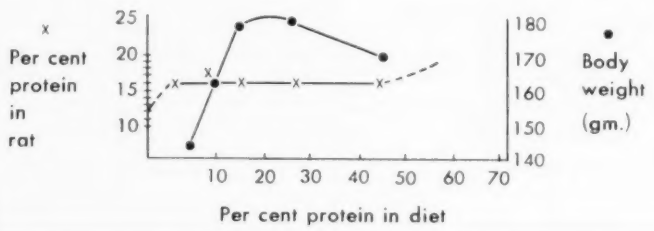


FIGURE 6.
(From Addis et al.[10])

It may be that other organs participate in increased nitrogen retention at high levels of intake. Not all tissues have been studied.

The next point I want to make is that the increment of nitrogen retained on the higher nitrogen intakes is a *labile fraction*. It is readily lost when the body is subjected to stress. There is an extensive literature dealing with this so-called toxic loss of nitrogen in both medical and surgical conditions, a phenomenon to which Cuthbertson,[17] Gross and associates,[18] and Howard and co-workers[19] have called particular attention. Does this labile nitrogen constitute a "protein reserve," something that can with advantage to the organism be drawn on in states of protein deprivation? The concept of a protein reserve, notably in the liver, is an old one, dating back to Pflüger[20] in 1903 and his pupil Seitz,[21] but it is still a prevalent concept. The chemical nature of "reserve protein" was extensively investigated by Luck[22] of Stanford some years back, who failed to find that any particular protein fraction was concerned.

Within the last decade, considerable attention has been paid to hepatic enzymes as constituents of labile liver protein, and it has been shown that hepatic enzymes as a whole vary directly with the protein intake.[23,24] Most of the observations have been made with low levels of intake, and we can guess that in this range deficiencies of enzyme function have practical importance. Observations made in kwashiorkor support this view. Nevertheless, we must be cautious in assuming that higher over-all enzyme activities are desirable, and indeed there is very little information as to what happens to enzymes when we go to the higher ranges of intake.

Some extraordinary paradoxes are known which make one hesitate to equate higher enzyme activities with better health. Not all enzymes vary directly with the protein intake. Although most are decreased on a reduced nitrogen intake, some are not at all affected and some are even increased. The more important enzymes, such as those concerned with oxidative phosphorylation, remain unaffected, according to Waterlow.[25] On low-protein intakes, hepatic desoxyribonuclease is somewhat diminished, according to Zigman and Allison,[26] but ribonuclease on the other hand is *markedly* increased. How are we to interpret that finding? Another interesting paradox concerns xanthine oxidase, an enzyme the activity of which in the liver varies directly with the protein intake. A notable lack of parallelism has, however, been observed[23,27] between these

TABLE 2

DISTRIBUTION OF BODY NITROGEN IN RATS WITH VARYING PROTEIN INTAKES*

PROTEIN IN DIET (PER CENT)	DISTRIBUTION OF BODY NITROGEN (PER CENT)				
	Kidney	*Liver*	*Heart*	*Uterus*	*Carcass*
6	0.60	4.0	0.36	0.13	85.4
11	0.59	4.6	0.36	0.18	84.8
16	0.63	5.1	0.38	0.18	83.6
27	0.67	5.2	0.39	0.19	83.8
43	0.72	5.0	0.33	0.19	83.7

*From Addis et al.[10]

TABLE 3

ORGAN WEIGHTS AND PROTEIN INTAKE IN PIGS*

DIET	WEIGHT OF ORGANS				BODY WEIGHT (KG.)
	Heart	*Kidney*	*Liver*	*Spleen*	
Low fat					
Protein 14 per cent	4.74	5.86	21.1	1.59	19.2
Protein 50 per cent	4.54	9.02	33.2	2.26	17.7
High fat					
Protein 14 per cent	4.53	6.19	23.3	1.77	19.6
Protein 50 per cent	4.26	7.19	32.4	1.93	23.0

*From Filer, Baur and Resbeck.[15]

TABLE 4

ORGAN COMPOSITION AND PROTEIN LOAD IN RATS*

PROTEIN IN DIET (PER CENT)	PROTEIN IN ORGANS (PER CENT)	
	Kidney	*Liver*
6	16.6	17.6
11	16.6	18.4
16	15.9	19.0
27	16.2	19.7
43	16.4	20.5

*From Addis et al.[10]

values and the ability of the animal during life to oxidize xanthine. We may also ask just how important xanthine oxidase is. The end product of purine metabolism varies in different animal species. In many, it is allantoin. In others, such as man and the Dalmatian dog, it is mostly uric acid; in a small segment of the human race (those with essential xanthinuria) it is xanthine rather than uric acid.[28] These individuals lead happy lives, however, in spite of their inability to oxidize xanthine. Most of them are discovered only by geneticists, occasionally by the passage of a xanthine calculus.

In summing up our knowledge of changes in body composition, as is done in table 5, it is apparent that we have no clear answer as to how much protein to feed. More significant information can be obtained by functional tests in which the animal fed different levels of protein is subjected to a variety of stresses. The practical question we want answered is this: *What diet will best protect the child from the stresses to which he is likely to be subjected?*

TABLE 5

SUMMARY OF CHANGES IN BODY COMPOSITION RELATED TO PROTEIN INTAKE

1. The so-called maturation of body tissue characteristic of early life (increasing per cent of nitrogen) can be accelerated by raising the protein intake.

2. A relation between this nitrogen accretion and functional maturation is not established.

3. The distribution of nitrogen in various organs is related to the work they are called on to perform in metabolizing protein.

4. The activity of many enzymes in the blood and tissues is affected in a variable manner by altering the protein intake; many are increased, a number are unaffected, and a few are decreased as protein intake rises. The most conspicuous changes occur in the less essential enzymes.

5. The concentration of free amino acids and the amino acid pattern of the free amino acids of the body cells may be considerably affected by the protein intake and the amino acid pattern of the diet.

Most of our information on this subject comes from animal studies, some of them conflicting and many of them inconclusive. Our knowledge is woefully incomplete. But such as it is I have attempted to review it and to add a few recent studies from our department at New York University College of Medicine.

Influence of Protein Intake on Resistance to Stresses

The various stresses that have been studied by different investigators are listed in table 6. I shall not attempt to present the data in detail. A schematic illustration of the general trend of the observations in the literature is shown in figures 7, 8, 9 and 10.

Physiologic stresses—The effect of protein on *growth* has been consistently obtained.[10,12,29] In the rat, maximal weight gain and body size are obtained with an intake of quality protein around 20 per cent. With levels above 40 per cent, growth falls off. *Sexual maturation* runs closely parallel to growth, but this does not hold for *reproductive efficiency*.[30] Reproductive performance reaches its peak at a level below that for maximal growth, after which it steadily declines. This holds for fertility in both sexes, the length of the reproductive span, and the mortality of the offspring. Lactation, on the other hand, improves steadily with increased protein intake.

The data on *longevity* in rats[31,32] must be interpreted with a certain amount of caution, for the causes of death differ to some extent from those of man. One must make some allowance for infections peculiar to the rat and for such conditions as a hair ball in the stomach. Nevertheless, significant data are obtainable, for, by and large, the causes of mortality of rats are not too different from those which affect humans. The general trend of the life span is quite similar to that for reproductive efficiency, the peak occurring well before that of maximal growth and steadily declining at higher protein levels. Observations on fish, too,[33] have shown that lower protein intakes are correlated with increased longevity.

The stresses of *exercise*, *heat* and *cold* have been of particular interest to military personnel, and many studies of diet and resistance to these stresses have been carried out. As far as protein is concerned, results of these investigations have been inconclusive.

Pathologic stresses—Infection—The conclusion is often drawn from abstract reasoning that better nutrition must of course mean better resistance to infection in general. This is one of the chief arguments for enriching and improving diet. However, as Schneider[34] pointed out, this theory is supported more by reiteration than by demonstration. An examination of the experimental data indicates that no such generalization can be made. The effect of protein varies with the particular infection. One must consider the effect of the diet on the parasite as well as on the host. The richer diet may benefit the host more or it may benefit the parasite more. In general, it would seem that in the case of a number of bacterial infections[35-37] a high-protein diet benefits the host rather than the parasite; in others such an effect is not demonstrable.[38] In viral infections,[39-41] there is evidence for the reverse effect. The subject has recently been reviewed by Clark and co-workers[42] and by Scrimshaw, Taylor and Gordon.[43]

The natural resistance of the host is another variable to be considered in dietary experiments. Thus Dubos and Schaedler[35] observed

TABLE 6

STRESSES STUDIED IN RELATION TO EFFECTS OF PROTEIN INTAKE

Physiologic stresses
Growth
Sexual maturation
Fertility
Exercise
Longevity
Physical agents
Heat
Cold
Irradiation
Pathologic stresses
Infections
Poisons
Neoplasms
Vascular disease
Dietary stresses
Deficiency of caloric food
Water deficiency
Protein deficiency

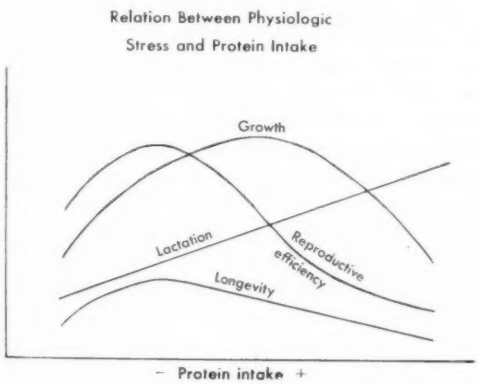


FIGURE 7.

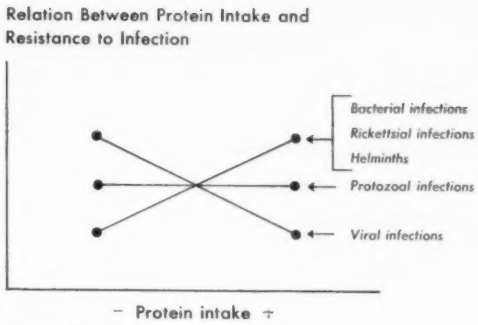


FIGURE 8.

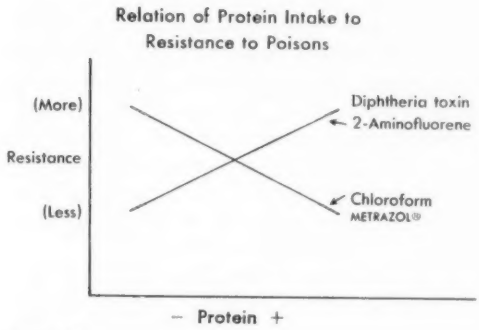


FIGURE 9.

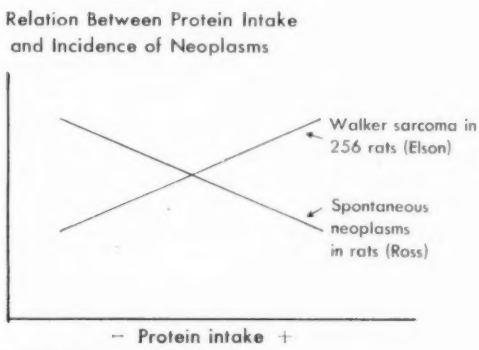


FIGURE 10.

a definite protective effect of protein against tuberculosis in a highly susceptible animal—the mouse—whereas in a relatively resistant animal—the rat—Metcoff and co-workers[43a] were unable to demonstrate this.

Poisons—The effect of diet on resistance to poisons is also extremely variable. Some poisons are best resisted on a high-protein diet,[44,45] some on a high-fat diet,[44,46] and some on a high-carbohydrate diet.[47]

The resistance to poisons is, however, not a simple phenomenon. More than one pathologic process may be considered, and these different processes are variously affected by the diet. Thus in the case of carbon tetrachloride poisoning it has been shown that a high-protein diet exerts some protective effect on the initial

TABLE 7

INFLUENCE OF DIET ON DEVELOPMENT OF SPONTANEOUS TUMORS IN 1000 RATS*

DIET	PROTEIN (PER CENT)	CALORIES PER DAY	INCIDENCE OF TUMORS (PER CENT)
High protein, high carbohydrate	30	58.5	40
Low protein, high carbohydrate	8	58.5	20
Low protein, low carbohydrate	8	22.5	2

*From Ross.[32]

parenchymal damage to the liver cell, although such a diet is deleterious during recovery, increasing the tendency to cirrhosis.[47a]

Neoplasms—There are instances in which individual tumors have particular requirements. One must consider the particular neoplasm in question. In the case of spontaneous tumors in rats and mice there is, however, a notable trend toward a higher incidence of tumors on the higher protein intakes. The long-term studies of Ross[32] in Delaware show this effect in a striking way (table 7).

Arterial disease—The relation between atheroma and diet is a subject which I should like to avoid in view of its highly controversial nature. As is well known, a number of different dietary factors have been incriminated. I shall confine myself to mentioning that several groups of investigators, notably Olsen and coworkers[48] in Pittsburgh, have shown a correlation with the protein intake (figure 11).

Ross[32] has not yet completed his long-term studies on rats fed different levels of protein, but his preliminary gross findings indicated that rigid "pipe-stem" aortas were seen particularly in the group receiving both high calories and high protein.

Halac[12] at New York University compared rats fed 27 per cent protein and 64 per cent protein in regard to resistance to a variety of stresses. The rats on the higher level were beyond the intake compatible with maximal gain in weight, and they weighed slightly less. Their bodies were, however, slightly higher in nitrogen, the kidneys showing the greatest increase (31%) above the controls (tables 8 and 9); the other viscera studied showed increases of 16 to 25 per cent.

The responses of these two groups to six different stresses have been studied to date. Swimming endurance in cold water and tolerance to x-ray, METRAZOL®, and food and water deprivation are shown in tables 10 to 14. In each experiment a better performance was obtained with the animals on the lower protein intake and the lesser "protein reserve." With the exception of the data on x-ray stress the results are statistically significant.

Most striking are the results of a study of the ability of the high-protein diet to protect the animal against the stress of protein deprivation. Here, if anywhere, the effect of a protein "reserve" should be demonstrable. The results shown in figure 12 failed entirely to demonstrate such an effect. When the two sets of animals were deprived of protein they both lost weight at the same rate. The first deaths occurred in animals on the high-protein intake, and when the experiment was terminated after 160 days of protein starvation only 39 per cent of these animals were alive, compared with 77 per cent on the lower protein intake.

One may ask why the animal that was richer in nitrogen did not perform better than he did. The answer is not hard to find. The animal on the high-protein intake loses nitrogen more rapidly when he is deprived than does the animal on the lower intake. This can be shown by balance experiments, as in the data of Filer and Baur on the pig (table 15). Protein turnover is more rapid on a high-protein diet, as has been demonstrated (figure 13) in the rat,[49] the dog[50] and in human adults.[51] The rapid turnover and the resulting loss of nitrogen appear to continue for some time after the nitrogen privation is instituted.

TABLE 8

CARCASS ANALYSIS OF WHOLE, UNSHAVED BODIES OF RATS

DIET	WATER (PER CENT)	FAT (PER CENT)	PROTEIN (PER CENT)	ASH (PER CENT)	SODIUM*	POTASSIUM*	CHLORIDE*
Normal protein (27 per cent)	62.5	14.8	17.7	3.1	18.5	29.9	12.1
High protein (64 per cent)	64.9	12.2	18.2	3.1	18.1	29.6	12.3

*Expressed in milliequivalents per 100 gr. fat-free solids (Filer, Baur and Resbeck[18]).

TABLE 9

WEIGHTS OF ORGANS EXPRESSED AS PERCENTAGE OF BODY WEIGHT

DIET	RATS (NUMBER)	BODY WEIGHT (S.D.)	LIVER	KIDNEYS	ADRENALS	TESTICLES	SPLEEN
Normal protein	15	478 ± 45	2.980 ± 0.651	0.516 ± 0.084	9.62 ± 1.44	0.687 ± 0.117	0.143 ± 0.032
High protein	15	429 ± 44	3.500 ± 0.450	0.677 ± 0.035	11.98 ± 1.83	0.795 ± 0.126	0.168 ± 0.047
p		0.05	0.02	0.01	0.01	0.05	0.02

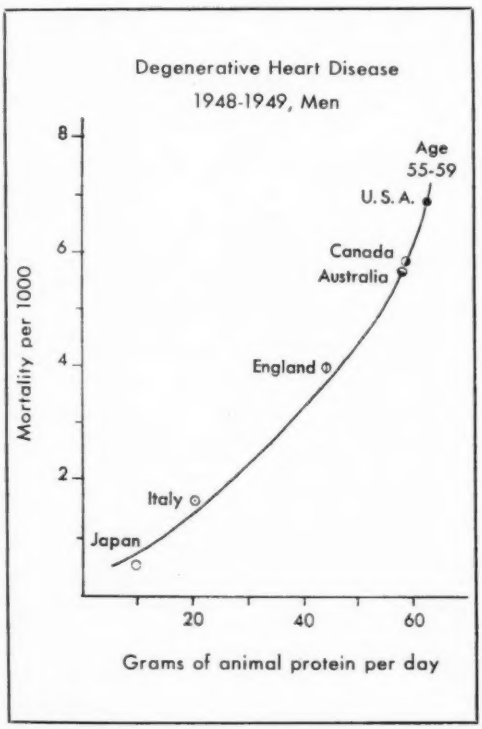


FIGURE 11.

I think we should abandon the term "reserve protein" and speak rather of "labile nitrogen" until we can at least demonstrate the protective effect that has been assumed.

Conclusions

What practical conclusions can we draw today from these studies in making recommendations for human protein intake? The limitations of our data even for the rat are obvious, and we have no precise formula for translating rat intakes into human intakes. About all we know is that a rapidly growing animal such as the rat requires more protein than does a more slowly growing one such as man. I would conclude that we should refrain from being guided by recommendations based on premises that are invalid. For many years maximal growth has been equated with optimum nutrition, the assumption being made that the diet which produced maximal growth must necessarily be the best to resist disease and other stresses. This seemed so obvious that no proof was needed. We have been impressed with the graph of the laboratory rat who gains weight more rapidly with a supplement of nutrient X, and we have been persuaded to put more X

TABLE 10

SWIMMING ENDURANCE IN WATER 5 TO 6° C.

DIET	RATS (NUMBER)	MEAN WEIGHT AND S.D.	AVERAGE ENDURANCE AND S.D. (SECONDS)	AVERAGE ENDURANCE (SECONDS PER GRAM BODY WEIGHT)
Normal protein	20	438 ± 57	503 ± 124	1.148
High protein	28	393 ± 36	425 ± 44	1.081

p 0.05

TABLE 11

RESISTANCE TO X-RAY STRESS

SERIES	DIET	RATS (NUMBER)	DOSE (ROENTGENS)	MEAN WEIGHT AND S.D.	MORTALITY
A	High protein	20	700	446 ± 41.3	3
	Normal protein	20	700	491 ± 66.5	3
B	High protein	15	800	468 ± 59.7	6
	Normal protein	15	800	549 ± 67.0	4

TABLE 12

MORTALITY FROM METRAZOL INJECTION

SERIES	DIET	RATS (NUMBER)	DOSE (MG./KG.)	SURVIVALS	
				Number	*Per cent*
A	Normal protein	10	50	6	60
	High protein	10	50	4	40
B	Normal protein	20	60	5	25
	High protein	20	60	3	15

$p < 0.7$

TABLE 13

SURVIVAL ON FOOD DEPRIVATION

DIET	RATS (NUMBER)	MEAN SURVIVAL AND S.D. (DAYS)	MEAN WEIGHT AND S.D.	
			Initial	*Final*
Normal protein	24	27 ± 8.5*	402 ± 41	208 ± 31
High protein	23	21 ± 4.3*	377 ± 35	216 ± 15

*$p < 0.05$

TABLE 14

SURVIVAL ON WATER DEPRIVATION

DIET	RATS (NUMBER)	MEAN SURVIVAL AND S.D. (DAYS)	MEAN WEIGHT AND S.D.	
			Initial	*Final*
Normal protein (27 per cent)	20	31 ± 5.24*	436 ± 38	176 ± 19
High protein (64 per cent)	26	26 ± 5.48*	382 ± 41	183 ± 28

*$p < 0.05$

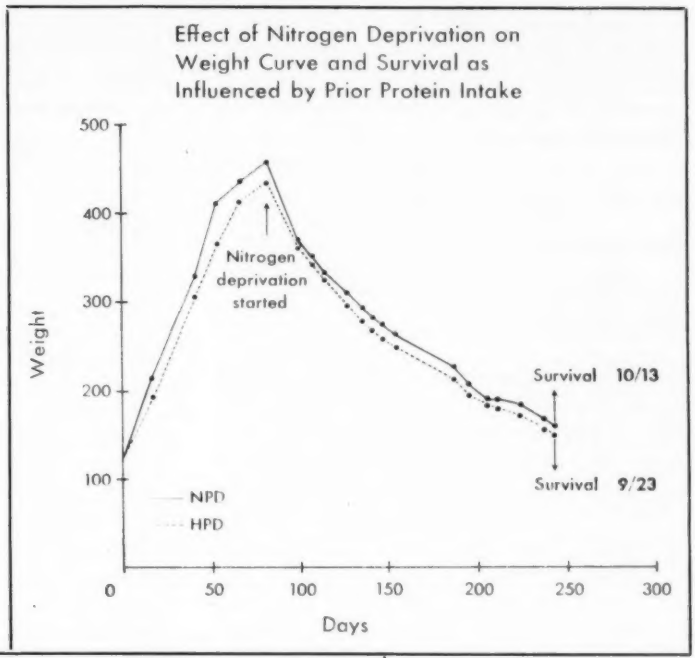


FIGURE 12.

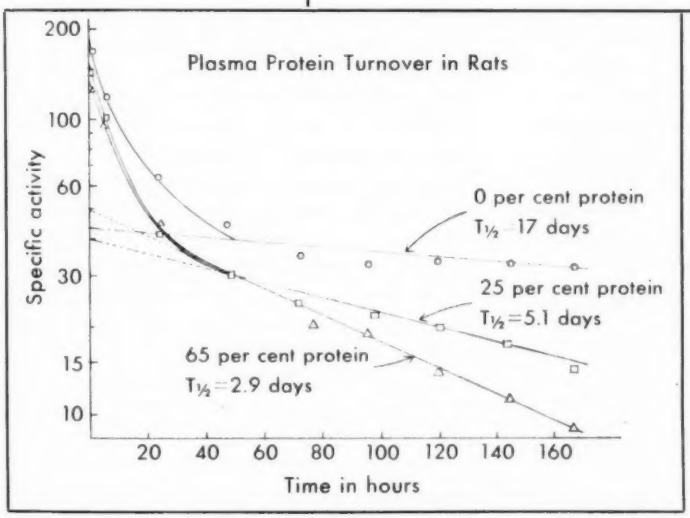


FIGURE 13.
(From Steinbock and Tarver.[59])

into our human diets. As a result our stature has been increasing. Harvard sons are now taller than their fathers and Vassar girls are taller than their mothers. The menarche comes a shade earlier. But has this resulted in better health?

If the animal data show anything, they show that no one diet is best for resistance to all stresses. What is best for one stress may be the worst for another. We have to think about what stresses are the most important for us and for our children—in the future as well as the present. We cannot predict what poisons our child is going to ingest, although a glance

TABLE 15

AVERAGE URINARY NITROGEN EXCRETION OF PIGS DURING STARVATION WITH AND WITHOUT WATER*

DIET BEFORE STARVATION	NITROGEN EXCRETION (GM./DAY)	
	No food or water	*Water only*
Low protein, high fat†	3.40	3.69
High protein, high fat†	6.11	4.68

*From Filer and Baur: Unpublished data.

†Four animals per group.

about the house might give us a clue. Perhaps we should concentrate on a diet that offers the best prospect of resistance to the atomic catastrophe that menaces us in the future. There is no question that size is a valuable attribute in certain careers, such as professional wrestling or being a barroom bouncer or the bodyguard of a future Al Capone. In college the big boy will be a more likely candidate for center on the football team; in school he has a better chance to achieve distinction as the class bully and a lesser chance of being the shrimp who is bullied. There are, however, disadvantages in size, too. In situations of per capita food rationing, the large individual who requires more fuel to stoke his body suffers more acutely.

Our chief concern is, however, that of resistance to disease. The animal work shows clearly that better resistance to one disease may mean poorer resistance to another. We still must determine the diseases against which we most want protection. A change in diet may result in a change in the pattern of disease in a population, and it is a matter of interest to determine whether a correlation can be found between the dietary pattern and the disease pattern of the population of the United States during the era of so-called newer knowledge of nutrition. The caloric intake and the distribution of calories in the United States have changed little. There has been a marked increase in vitamin intake. The changes in protein consumption, our present concern, are shown in table 16, compiled by the United States Department of Agriculture.[52,53]

TABLE 16

DIETARY PATTERN IN THE UNITED STATES*

PROTEIN IN DIET	YEARS	
	1909-1913	*1956*
Intake per capita (grams per day)	102	97
Animal protein (per cent)	51.9	67.6
Other sources of protein (per cent)		
Dairy products	17.7	25.5
Eggs	5.2	6.8
Meat, poultry, fish	29.0	35.5
Cereal products	35.7	19.6
Legumes, nuts	4.5	5.1
Other vegetable sources	7.9	7.7

*From Handbook No. 62, U. S. Department of Agriculture, 1957.[52]

TABLE 17

CHANGING PATTERN OF DISEASE IN THE UNITED STATES

DECLINING OR DISAPPEARING DISEASES	EMERGING OR APPEARING DISEASES
Bacterial infections	Viral infections
Tuberculosis	Neurotropic
Syphilis	Respiratory
Typhoid	Allergy
Diphtheria	Collagen diseases
Pneumonia	Neoplasms
Streptococcal infections	Atheroma, coronary occlusion
Scarlet fever	
Erysipelas	
Rheumatic fever	
Infantile diarrhea	

Animal protein has made notable gains, chiefly at the expense of cereals. Although the total protein intake has not been changed, the increase in protein quality is equivalent in its effect to an increased protein intake, and it may well be that this change has been responsible for the increasing stature. Table 17 shows the changes which have occurred in the disease pattern in the United States during this period of protein enrichment of our diet.

Infectious diseases, particularly those of bacterial etiology, have declined in importance. Among the diseases which have assumed a prominent place are neurotropic viral infections, allergy and the collagen, vascular and neoplastic diseases. A positive correlation between two variables does not establish a relationship between them. We know of other factors that undoubtedly have had an influence on the disease picture. Our antibiotic drugs have decreased or eliminated many bacterial

fections, and the survivors who succumb to arterial or neoplastic disease in later life are to some extent a selected group. Diagnosis, too, has been improved and neoplastic disease is now more frequently recognized. It is impossible to disentangle these variables in mortality and morbidity statistics. On the other hand it seems a little more than a coincidence that so many of the diseases that are emerging on the American scene are those which in animals are associated with a high-protein intake.

In the light of our present uncertainties and the suggestive evidence that we may have passed the optimum protein intake for meeting some of our important stresses, are we justified in continuing to enrich our diets with protein? The pressures to do so are great. The cereal industry has become protein-conscious and has begun to reinforce its products with protein and amino acids. Protein content and protein quality have become sales gimmicks in the food industry. As doctors we want to play it safe and to subject our patients to the least possible risk. But is it playing it safe to go along with this trend, or is it time we called a halt until we can evaluate what our present diets are doing before we go further along the road of protein "enrichment"?

There are signs that a new point of view is making some headway in nutritional circles. The dominant thinking for several decades now has been expressed by the Food and Nutrition Board of the National Research Council with its table of recommended allowances of nutrients. This table was based on the concept that an insufficiency of one or another nutrient constituted the only dietary risk. Recommended allowances were therefore made generous to cover possible insufficiency by a wide margin of safety; no consideration was given to possible consequences of an overgenerous supply. A somewhat different point of view has been taken by the recently organized committee of the armed services, the ICNND (Interdepartmental Committee on Nutrition for National Defense[54]). The dietary tables proposed by this group list four levels for each nutrient. Maximal as well as minimal levels are considered; a margin of safety for both high and low intakes is regarded as desirable. Possibly the unexpectedly high incidence of atheroma found in autopsies of "well-fed" American soldiers who died in the Korean war was a factor in this change of thinking. The ICNND has not as yet published nutrient tables for children but such tables are said to be in preparation.[55] I believe that this is a healthy development.

I shall try to emphasize my final point with a story about four men—an Englishman, a Frenchman, a Pole and an American—who agreed to write an essay on the subject of elephants. The Englishman wrote on "Elephants that I have hunted"; the Frenchman on "L'Eléphant et ses amours." The Pole (who wrote in French) turned in an essay entitled "L'Eléphant et la question polonaise," but the American wrote about "Bigger and better elephants." Being an American I, too, am all for the bigger, but I would like to be sure that in the nutrition field what we are getting is *better*, not just *bigger*.

REFERENCES

1. Orr, J. B. and Gilks, J. L.: Studies of nutrition; the physique and health of two African tribes. Special Report No. 155. Medical Research Council. London, H. M. Stationery Office, 1931.
2. Swanson, W. W.: The composition of growth. II. The full term infant. Am. J. Dis. Child. 43:10 (January) 1932.
3. Fomon, S. J. and May, C. D.: Metabolic studies of full term infants. Pediatrics 22:101, 935, 1958.
4. Wallace, W. M.: Nitrogen content of the body and protein reserve. Fed. Proc. 18:1125, 1959.
5. Moulton, C. R.: Age and chemical development in mammals. J. Biol. Chem. 57:79, 1923.
6. Snyderman, S. E. et al.: Observations on high and low protein diets. A.M.A. J. Dis. Child. 96:631, 1958.
7. Gordon, H. H., Levine, S. Z., Wheatley, M. A. and Marples, E.: The nitrogen metabolism in premature infants. Am. J. Dis. Child. 54:1030, 1937.
8. Talbot, N. B. et al.: Functional Endocrinology From Birth Through Adolescence. Cambridge, Harvard University Press, 1952, p. 456.
9. Cusworth, D. C. et al.: Free amino acids in erythrocytes of infants. (Abstract.) Fed. Proc. 18:209, 1959.
10. Addis, T., Lee, D. D., Lew, W. and Poo, L. J.: The protein content of organs and tissues at different levels of protein consumption. J. Nutrition 19:199, 1940.
11. Garrow, J. S.: Effect of protein depletion on distribution of protein synthesis. J. Clin. Invest. 38: 1241, 1959.
12. Halac, E., Jr.: The effect of high protein diets on

resistance to stress. Report to Ninth International Congress of Pediatrics, Montreal, 1959. (To be published.)
13. Tepperman, J., Engel, F. L. and Long, C. N. H.: Effect of high protein diets on size and activity of adrenal cortex in the albino rat. Endocrinology 32: 403, 1943.
14. Leatham, J. H.: Adrenal and thyroid weights in rats following high protein diets and testosterone propionate. Exper. Med. & Surg. 9:138, 1951.
15. Filer, L. J., Baur, L. S. and Resbeck, H.: Influence of dietary protein and fat on the body composition of piglets. J. Nutrition. (In press.)
16. Walter, F. and Addis, T.: Organ size and organ work. J. Exper. Med. 69:467, 1939.
17. Cuthbertson, D. P.: Observations on disturbance of metabolism produced by injury to limbs. Quart. J. Med. 1:233, 1932.
18. Gross, C. M. et al.: Nitrogen metabolism in acute infections. J. Clin. Invest. 24:523, 1945.
19. Howard, J. E. et al.: Studies on fracture convalescence. Bull. Johns Hopkins Hosp. 75:156, 209, 1944.
20. Pflüger, E.: Glycogen. Arch. ges. Physiol. 96:381, 1903.
21. Seitz, W.: Die Leber als Vorrathskammer fur Eiweisstoffe. *Ibid.* 111:309, 1906.
22. Luck, J. M.: Liver proteins; question of protein storage. J. Biol. Chem. 115:591, 1936.
23. Knox, W. E., Auerbach, V. H. and Lin, E. C. C.: Enzymatic and metabolic adaptations in animals. Physiol. Rev. 36:164, 1956.
24. Waterlow, J. C.: Protein nutrition and enzyme changes in man. Fed. Proc. 18:19, 1959.
25. ——: Report to Ninth International Congress of Pediatrics, Montreal, 1959.
26. Zigman, S. and Allison, J. B.: Ribonuclear activity in tumor-bearing and protein-depleted rats. (Abstract.) Fed. Proc. 18:359, 1959.
27. Westerfeld, W. W. and Richert, D. A.: Acetaldehyde utilization by protein-depleted dogs and rats. Proc. Soc. Exper. Biol. & Med. 87:524, 1954.
28. Dent, C. E. and Philpot, G. R.: Xanthinuria—an inborn error (or deviation) of metabolism. Lancet 1:182, 1954.
29. Slonaker, J. R.: Effect of different percents of protein in diet; growth. Am. J. Physiol. 96:547, 1931.
30. ——: Effects of different percents of protein in diet; reproduction. *Ibid.*, 97:322.
31. ——: Effect of different percents of protein in diet; life span and cause of death. *Ibid.*, 98:266.
32. Ross, M. H.: Proteins, calories and life expectancy. Fed. Proc. 18:1190, 1959.
33. McCay, C. M., Dilley, W. E. and Crowell, M. F.: Growth rates of brook trout reared on purified rations. J. Nutrition 1:233, 1929.
34. Schneider, H. A.: Nutrition and resistance to infection. The strategic situation. Vitamins & Hormones 4:35, 1946.
35. Dubos, R. J. and Schaedler, R. W.: Effect of dietary proteins and amino acids on susceptibility of mice to bacterial infections. J. Exper. Med. 108:69, 1958.
36. Ratcliffe, H. L. and Merrick, J. V.: Tuberculosis induced by droplet nuclei infection—its developmental pattern in hamsters in relation to levels of dietary protein. Am. J. Path. 33:107, 1957.
37. Miles, J. A. R.: Observations on the course of infection with certain natural bacterial pathogens in rats on protein deficient diets. Brit. J. Exper. Path. 32:285, 1951.
38. Schneider, H. A. and Webster, L. T.: Nutrition of host and natural resistance to infection. J. Exper. Med. 81:359, 1945.
39. Jones, J. H., Foster, C., Henle, W. and Alexander, D.: Effects of low protein and of low tryptophan diets on the susceptibility of mice to the Lansing strain of poliomyelitis virus. Arch. Biochem. 11:481, 1946.
40. Sprunt, D. H. and Flanigan, C. C.: The effect of malnutrition on the susceptibility of the host to virus infection. J. Exper. Med. 104:687, 1954.
41. Myrick, G. S. and Leftwich, W. B.: Effect of diet on susceptibility of the mouse to pleuropneumonia virus (PVM). *Ibid.* 89:155, 1949.
42. Clark, P. F. et al.: Influence of nutrition on experimental infection. Bact. Rev. 13:99, 1949.
43. Scrimshaw, N. S., Taylor, C. E. and Gordon, J. E.: Interactions of nutrition and infection. Am. J. M. Sc. 237:367, 1959.
43a. Metcoff, J. et al.: Nutritional status and infection response; electrophoretic, circulating plasma protein, hematologic, hematopoietic and pathologic responses to Mycobacterium tuberculosis (H 37 RV) infection in protein-deficient rat. J. Lab. & Clin. Med. 34:335, 1949.
44. Meyer, A. R.: Influence of diet on resistance. Proc. Soc. Exper. Biol. & Med. 41:402, 406, 1939.
45. Sako, W.: Resistance to infection as affected by variations in proportions of protein, fat and carbohydrate in the diet; experimental study. J. Pediat. 20:475, 1942.
46. Craven, E. G., Jr.: Importance of diet in preventing acute yellow atrophy during arsphenamine treatment. Bull. Johns Hopkins Hosp. 48:131, 1931.
47. Opie, E. L. and Alford, L. B.: Influence of diet on hepatic necrosis and toxicity of chloroform. J.A.M.A. 62:895, 1914.
47a. Sriramachari, S.: Nutritional factors in the pathogenesis of cirrhosis. Indian J. Path. & Bact. 1:35, 1958.
48. Olsen, R. E., Jablonski, J. R. and Taylor, E.: Effect of dietary protein, fat and choline upon the lipids and lipoproteins of the rat. Am. J. Clin. Nutrition 6:111, 1958.
49. Steinbock, H. L. and Tarver, H.: Plasma protein. V. Effect of protein content of diet on turnover. J. Biol. Chem. 209:127, 1954.
50. Yuile, C. L. et al.: Plasma protein turnover and tissue exchange. J. Exper. Med. 109:173, 1959.
51. Iber, F. L. et al.: Effect of level of dietary protein and L-triiodothyronine on catabolism of radioactive iodinated serum albumin. J. Clin. Invest. 37:1442. 1958.
52. Consumption of Food in the United States (1909-1952). Handbook No. 62. Washington, D. C., U. S. Department of Agriculture, 1953.
53. *Ibid.* (Supplement), 1956.
54. Interdepartmental Committee on Nutrition for National Defense: Manual for Nutrition Surveys. Bethesda, National Institutes of Health, 1957, p. 123.
55. Woodruff, C. W.: Personal communication to the author.

Self-help Devices:

Aids to Telephoning

EDWARD W. LOWMAN AND HOWARD A. RUSK

Institute of Physical Medicine and Rehabilitation
and the Arthritis Self-help Device Office*

New York University Medical Center, New York

DAILY use of the telephone requires a degree of facility in all muscles and joints of the upper extremities. One must have the ability to reach and grasp, have sufficient strength to lift and maintain a hold on the handset, and have adequate finger dexterity to dial a number. Impaired speech and hearing can also be deterrents to successful use of the telephone.

This article, the first of two on telephone aids, considers devices requiring completely revised service, which accommodate extremely disabled persons. The Bell Telephone System offers many ingenious solutions to complex problems, some of which are illustrated here. Installations approved by the telephone company insure prompt maintenance should the mechanism fail; therefore, it is advisable to consult the local service before installing a device that might ultimately have a deleterious effect on and impair the level of transmission.

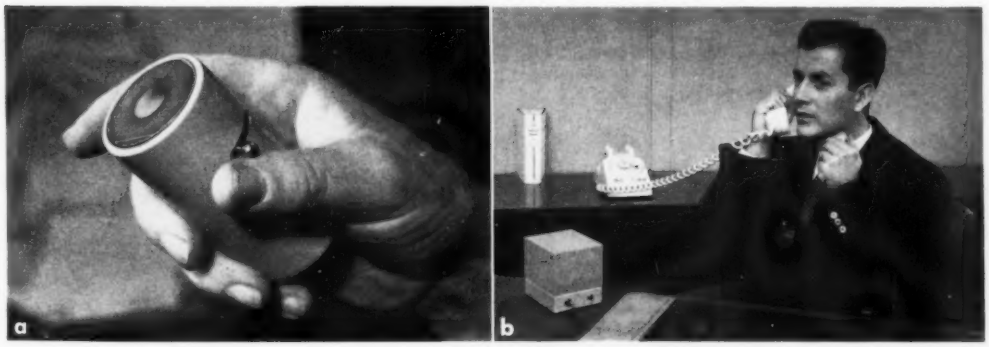


FIGURE 1. Although many persons who have lost the use of their vocal cords can learn to communicate by esophageal speech, some are unable to do so.

a. The Electronic Larynx utilizes a modified telephone receiver to transmit sound through flesh into the throat. By manipulating a pitch-control switch while talking, the user can make his artificial voice sound quite natural.

b. D. J. MacLean, one of the developers of this device, demonstrates its use with a telephone.

The National Hospital for Speech Disorders and the Bell Telephone System have collaborated in designing this instrument.

*Supported at the Institute by the Arthritis and Rheumatism Foundation.

FIGURE 2. This unit aids those with impaired speech and hearing. A bar in the transmitter amplifies the voice when the handset is removed from the cradle. A button on the base of the set increases the volume of the voice of the person at the other end of the line. (Bell Telephone Laboratories.)

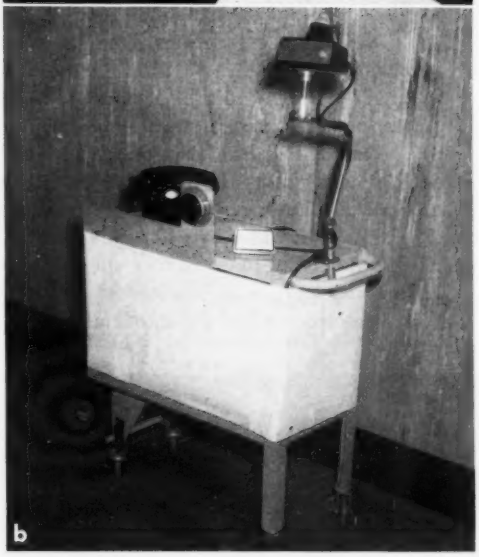


FIGURE 3. The Speakerphone, a precision instrument with microphone and loudspeaker, provides "hands-free" communication within normal range.

a. To use the unit one needs only to push an "On" button for answering a call and an "Off" button for disconnecting. Dialing outside calls is necessary unless special arrangements are made through the telephone company for a direct line to the operator. (Bell Telephone System.)

b. A special portable mobile Speakerphone with a single "On-off" button control is easily operated. (New York Telephone Company.)

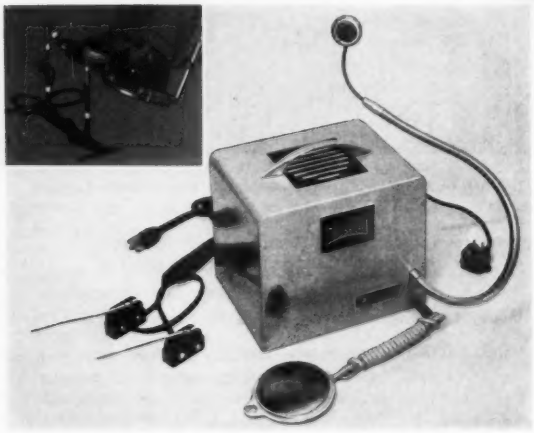


FIGURE 4. The Rehabaphone accommodates persons with little or no muscle power. The unit can be operated by muscles used for smiling, winking, bulging the cheeks, and closing the mouth or by minimal motion of the chin, foot *(inset)* or hand. Made by Seeger-Williams, Inc., 4 Norman Street, Bridgeport 5, Connecticut.

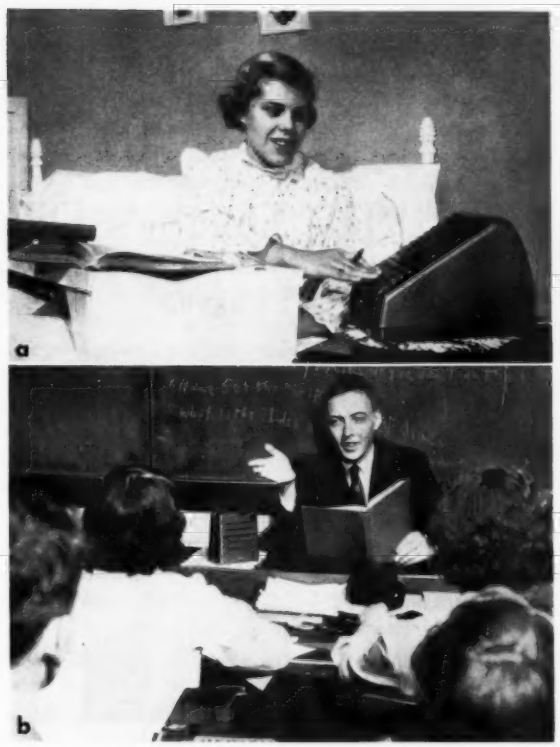


FIGURE 5. An electronic intercommunication unit especially engineered for use with telephone lines enables the homebound pupil to participate in classroom activity throughout the school day.

The pupil speaks through the home unit (a) by pressing a talk switch. The voice is carried over private telephone lines to an amplifier and is received by a stationary or portable unit located in the classroom (b).

This equipment is made by Executone, Inc., and furnished nationally by the Bell Telephone System and independent companies. Write to J. A. Richards, Educational Director, Executone, Inc., 415 Lexington Avenue, New York 17, for handbook.

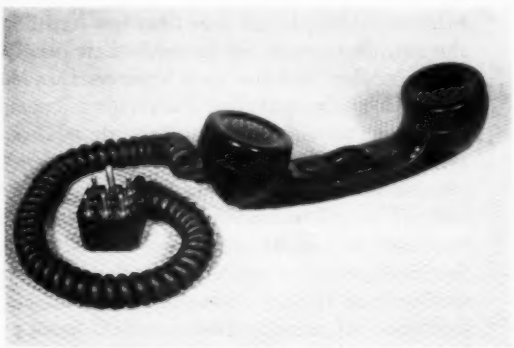


FIGURE 6. Only the slide "Off-on" button switch mounted in the hollow handle differentiates this telephone handset from the conventional set. Because it is small and compact, the unit may be placed on the bed without discomfort to the patient. (Bell Telephone System.)

The cost of installing and maintaining any of the devices illustrated here is variable, depending on the specific device and modifications needed. Write directly to the Bell Telephone System or the listed manufacturers for further information. The second article on telephone aids will show simple, commercially available devices for reducing stress and improving function in using a standard telephone.

Readers are invited to submit suggestions and ideas for devices they have developed and would like to share with others. Forward all such suggestions and comments to: Editorial Department, POSTGRADUATE MEDICINE, Essex Building, Minneapolis 3, Minnesota.

The Doctor's Dilemma

I. S. RAVDIN*

University of Pennsylvania School of Medicine, Philadelphia

I. S. RAVDIN

I AM honored that you have asked me to come here today to participate in these exercises, and that you have made me an alumnus of this great university. No other honor that I can think of would have made me leave the meeting of the Clinical Congress of the American College of Surgeons in Atlantic City. That great College has always received a high measure of its stimulus from men who were connected with the school of medicine at Northwestern: Allen Kanavel, whom I remember as a boy courting Olive Rosenkranz who lived across the street from me in Evansville, Indiana; Sumner Koch; Michael Mason; and your distinguished Chairman of the Department of Surgery, Loyal Davis, who has done so much for the American College of Surgeons and who among his many accomplishments has elevated *Surgery, Gynecology and Obstetrics* to the highest position of any surgical journal in the world.

I wish to discuss with you a few of the many problems which now concern American medicine. Some of them have been with us for a long time; others are of more recent origin. All of them are of considerable concern to those who, in one way or another, are playing a part in the destinies of the medical profession. And since a satisfactory solution of many of these matters is of concern to our people, we must earnestly attempt to find a reasonable solution for them.

In 1900, the three most common causes of death were tuberculosis, pneumonia and infantile diarrheas. At that time one-fourth of the newborn would fail to reach their twenty-fifth birthday, and now only 5 per cent are not likely to attain that age. Tuberculosis, pneumonia and the infantile diarrheas are not even among the first 10 causes of death. Epidemic diseases in this country of a serious nature are now nearly unheard of. Even the influenza epidemic of several years ago claimed but a few lives when compared with the influenza epidemic of 1918. Poliomyelitis, even though it is not yet completely controlled, need no longer be the dreaded disease that it was. Smallpox is of the greatest rarity. The streptococcal infections, which have caused such serious derangements of the heart, can now in large part be prevented.

While surgeons will be working for some years overcoming the valvular defects which such infections have previously caused in so many of our people, we can look forward to a substantial reduction of these disabling disorders in the future.

*Professor and Chairman of the Department of Surgery, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania.

This address was presented at the Centennial Celebration, September 29, 1959, of Northwestern University Medical School, Chicago, Illinois, and is reprinted with permission from the *Quarterly Bulletin* of Northwestern University Medical School.

Aneurysms of the larger blood vessels can now be removed with a remarkably low mortality. While we have not had as many important advances in the field of malignant disease as we should have liked to have made, progress in this area is being recorded. Patients with malignant disease whose lesion can be removed before spread has taken place can be cured; and even those in whom spread has taken place have a reasonable chance of prolongation of life by means of radical surgery, irradiation and chemotherapy.

Our major tasks are to unravel the nature and causes of malignancy, to develop specific tests for its detection, and to find better methods of therapy for many malignant tumors. In spite of all the splendid fundamental and clinical research which is being done in this country, the practitioner finds it difficult to sift the wheat from the chaff, and the families of those suffering from widespread malignant disease wonder whether members of the medical profession are withholding information of value in the treatment of these patients.

It is, of course, unthinkable that dedicated investigators would do this, but many of our people are not convinced that this is true. Certain members of the medical profession have wittingly or unwittingly encouraged our people in this belief.

In August of 1939, Professor Florey came to Philadelphia from England to see Dr. Alfred Newton Richards. The world was on the threshold of war, and Florey wished to discuss certain problems with him for the British Medical Research Council. I had the opportunity of having dinner with the two of them. Professor Florey told us at some length of the isolation of penicillin by Fleming. When Dr. Richards suggested that large amounts of this be made for clinical trials, he was told that the British were too involved to do this on a high priority. Dr. Richards solved this problem, which was so important to people, by interesting Americans in making penicillin. Dr. Chester Keefer was made responsible for the clinical trials of the newly made antibiotic. In the effort to cure a variety of infections, large amounts of this antibiotic were administered to the sick and injured. The war was hardly over before more antibiotics became available and were used in a wide variety of disorders without consideration of their real usefulness. In spite of the fact that bacterial geneticists very early warned the medical profession that they must understand the basic laws of bacterial behavior, it was not very long before we were faced with organisms which, while initially vulnerable to these newly found agents, had because of indiscriminate use become resistant to them.

Now in this country, and in all the civilized countries of the world where medicine is practiced at a supposedly high level, we have these resistant strains or mutations which are resistant to all but a very few of the now available antibiotics. Certain of the resistant strains of staphylococci now account for a considerable number of the deaths occurring in many of our hospitals each month. The doctor's dilemma concerns itself with the fact that these resistant strains are the result of our own carelessness. Before we find the final answer to this serious problem, we may well have lost as many people from infections resistant to the antibiotics as have lost their lives in certain of our wars. The tragedy of it all is that many patients still insist on receiving these agents which are capable of producing as much harm as the good they do when properly given.

Paul R. Hawley, the staunch Director of the American College of Surgeons, recently gave a paper in New York entitled "Quality as well as quantity." A good many people objected to what he said on the basis that he was saying things that might be said to doctors only but not to the lay public. I would hasten to call your attention to the fact that the health of any people is dependent first on the quality of the medical profession serving them. Our population is increasing so rapidly that if we are to maintain our present standards of patient care, we shall have to have more doctors, and we have every right to expect that the quality of our practitioners will remain as good as it is today.

The simple truth of this matter is that by 1970 to 1975, when the population of this country will approach 235 million people, we shall have to be graduating approximately one-third more doctors than we are graduating

now. This will require the equivalent output of 20 new medical schools with all that this would entail. This is a dilemma which faces us as a profession and the nation as well.

In the university with which I am associated, the cost of tuition in the medical school has increased about 175 per cent since I was a student. This seems like an extraordinary increase in cost, but I would call your attention to the fact that tuition fees in spite of their constant increase, year after year, have not kept pace with medical school budgets.

And while we are talking about the need for additional graduates from our medical schools, we must keep in mind that at any time we might become involved in warfare. Recent meetings of the Radiation Subcommittee of the Joint Committee on Atomic Energy have brought out some interesting findings. The testimony related largely to a so-called limited attack using 1,453 megatons of nuclear bombs on 224 targets in this country. One megaton, as you know, is equivalent in its explosive power to one million tons of TNT. My friends who are physicists tell me that 1,453 megatons would really be a modest attack, and yet the net results of such an attack would result in 48 million people being killed, 20 million being injured, 25 per cent of the nation's homes destroyed, and an additional 25 per cent of homes damaged. In the 30 succeeding generations between 24 and 960 million descendants of the survivors would be born with genetic faults as the result of the nuclear radiation to which their ancestors were exposed.

Graduating from a medical school is not all that the young man must achieve. He must have an internship, if possible in one of our better approved hospitals. Very few of these institutions pay very much for this service, and following the completion of the internship, a considerable number of the graduates, as high as 90 per cent, wish to receive residency training in one aspect of medicine or surgery or their specialties. This may take from two to five years, during which time they are also paid a totally inadequate salary. A great many of these young men are married and have children at the time they are receiving special training. The net result of all this is that when the individual is ready to go into practice, he is deeply in debt. He spends a number of years paying his debtors before he can begin to provide security for himself and his family.

Although there can be no doubt that some physicians and surgeons overcharge their patients, the majority of them are dedicated to their work. The late Senator Richard L. Neuberger once quoted the wife of a student at the University of Oregon School of Medicine regarding this matter as follows: "Most people don't know about the sacrifice which goes into a medical career." If we are to continue to have the best of our young men seek a career in medicine, we shall have to do something about this very important matter.

We must search further to ascertain why it is that many of the best of our young men are not going into medicine. The emphasis at the present time is on science, mathematics, chemistry and physics. Only a few years ago these individuals were entering medical training. We have accomplished so much in the past for the health of our people. Why is it that we do not attract, at the present time, the best of our young men?

Recently a statement was prepared by the President's Science Advisory Committee entitled "Education for the age of science." In the introduction of this statement one finds the following: "Today in America we need a very wide variety of human talent. We need not only farmers and artisans, clergymen and lawyers; we need also painters, sculptors, nuclear scientists, business leaders, engineers, architects, economists, bankers and politicians. We need a host of other kinds of people, each with special training but all with a broad background and point of view." One finds in this statement a singular lack of appreciation of the medical profession.

Too often we talk of our medical schools in terms of the buildings they have and the budgets that are available. The time has come when we must examine more closely the educational experiences we are offering those who are studying medicine. Buildings and budgets and even curricula are not necessarily all-important. The experience and the knowledge the student gains during his period of train-

ng are after all of primary importance. We must be sure that we are constantly stimulating the intellectual curiosity of our students. We must be sure that the educational experience we provide will constantly stimulate them to continue to enrich their fundamental training. If we do this we shall feel sure of the fact that they will maintain an interest in the developing aspects of medicine in the future.

I have previously said in Chicago that the introduction of any plan tending to the socialization or control by government of medical education and practice will lead to the control of other professional activities at the same level. I am convinced that those who are storming and attempting to capture the citadel of medical practice are doing so because this provides the simplest mechanism for changing the entire democratic philosophy on which this country was founded. Dr. James B. Conant, at one time president of Harvard University and later High Commissioner in Berlin, stated a few years ago: "For just as the study of pathological conditions in plants and animals may throw light on the conditions required for healthy growth, so, too, a study of Communist doctrine may be useful in an analysis of the role of our scholarly institutions in the free world. By realizing what happens when the citadel of learning has been captured, we may be better able to understand what is the essence of the activities within this citadel when it remains free."

We must find a satisfactory solution for the deterioration of the doctor-patient relationship. We must ascertain why it is that certain members of our profession fail to heed section four of the Principles of Medical Ethics as adopted by the American Medical Association which reads as follows: "The medical profession should safeguard the public and itself against physicians deficient in moral character or moral competence. Physicians should observe all laws, uphold the dignity and honor of the profession, and accept its self-imposed discipline. They should expose without hesitation, illegal or unethical conduct of fellow members of the profession."

We must ascertain why it is that the number of malpractice suits is constantly on the increase. Is it not possible that this is in part due to a constant deterioration of the doctor-patient relationship?

We must agree that the cost of medical care has increased sharply, but we must also point out that doctors are not solely responsible for these added costs. The greatest increase in costs has come from increase in hospital costs and from the increase in the cost of newer pharmaceuticals that are often so important for the care of people.

It is not too difficult to see that we have a great many serious problems which now face us. Some of them start in the medical school and others are added on our way through life. Some of these we have found answers to, but there still remain a great many for which we have not been able to prescribe adequate therapy. There can be no doubt that our relationships with patients are not as good as they once were. The methods we have used for creating a better atmosphere of understanding between those practicing medicine and the general public need a very careful overhauling.

We must, however, admit that all is not well with us. While new knowledge is developing at an unbelievable rate, there are changing concepts of community service which have raised serious problems for our profession. Medicine is experiencing a vast number of changes which involve and affect its total structure and operation. We must inquire seriously into the motivation, the nature and the direction of those changes.

We should, as rapidly as possible, gain insight into the significance and meaning of these changes, which medicine in a free country is experiencing. We must ask ourselves, "What is happening in and to medicine? What are the immediate and foreseeable effects on medicine and society?"

We must not lose sight of the age-old concept of the doctor as a member of a dedicated profession. We must under no circumstances resort to practices which we would condemn when used by our adversaries. We must constantly remind ourselves that under somewhat similar circumstances Cicero stated 2000 years ago, "Our customs have perished for want of men to stand by them."

Editorials

Postgraduate Medicine

Editor-in-Chief:
CHARLES W. MAYO, M.D.

Contributing Editor:
MORRIS FISHBEIN, M.D.

Executive Editor:
SYLVIA COVET

WHAT'S HAPPENING TO OUR WARD ROUNDS?

Is it possible to increase the therapeutic value of ward rounds without impairing their teaching value? This question assumes added significance in light of the results of a recent study made by liaison psychiatrists assigned to the medical and surgical services of a voluntary hospital. Patients were interviewed by the psychiatrist as soon as possible after being examined by the staff so that their impressions would still be fresh. The questions were designed to elicit patients' reactions both to the general situation and to any special circumstances that might have been present.

It soon became apparent that the patients' reactions to medical rounds differed greatly from their reactions to surgical rounds. Medical rounds were, on the whole, not traumatic to the patients because the medical staff exercised a greater degree of discretion than did the surgical staff in respect to what they said in the presence of the patients. Medical rounds were conducted in a comfortable manner and were generally free from tension. The patients seemed able to control their anxiety by not acknowledging the seriousness of their illness. No intern or resident was criticized in the presence of a patient; the members of the house staff appeared to feel free to ask questions and to express opinions that differed from those of the attending staff.

Surgical rounds, on the other hand, often left the patients in a state of agitated uncertainty as to their condition and their outlook for recovery. The use of disturbing diagnostic terminology and the discussion of animal experimentation and morbidity and mortality statistics in the presence of patients served to confuse and depress them. In many instances interns or residents were openly chided by the attending staff. The patients were disturbed when they heard their doctor being scolded or humiliated by his superiors. The feeling was missing that both older and younger doctors were working together as a team for the patients' benefit.

It was discovered that the patients regarded differences of opinion on procedure or diagnosis before operation as a good sign, but that differences of opinion after operation as to what procedure should have been used were disturbing. Many patients complained of a

lack of respect for their privacy on the part of the doctors during open examination of incisions, intestinal stomas and so forth.

It appears obvious from this study that if care is not exercised to prevent it, a "hierarchy" develops in the surgical service in which the echelons of higher rank and status have rights and prerogatives not allowed those immediately below them. This situation should not exist among colleagues who, despite differences in age and rank, are, after all, equal in respect and professional dignity. One study revealed that in a large municipal hospital the situation between the house staff and the attending staff became so aggravated that several patients, upset by the disagreements, signed out of the hospital, against advice, after the surgical rounds were concluded.

What then can be done to enhance the therapeutic value of surgical ward rounds without damaging their teaching value? The results of this study would seem to indicate a need for the following procedures: (1) exploiting the position of respect which the attending surgeon occupies in the eyes of the patient; (2) exercising care to see that all disturbing discussions, reprimands or open disagreements are conducted out of earshot of the patient; (3) maintaining respect for the patient's privacy while the examination is in progress; (4) limiting, whenever possible, examinations which would be painful to the patient; and (5) creating a friendly, relaxed atmosphere by answering the patient's questions and by including him in the discussion whenever it is practical to do so.

Careful re-examination of the procedures in surgical ward rounds is mandatory if these apparent abuses and archaic practices are to be eliminated.

ROBERT TURELL

THE HOSPITAL'S FIGHT FOR SURVIVAL

TODAY the United States, through the Hill-Burton Act and through its continued prosperity, has developed great numbers of new hospitals. This is in contrast to what has gone on in Great Britain, where new hospitals have not been built since 1937. Now, however, an act of Parliament has provided funds for some remodeling of old hospitals and for the building of a few new structures. In the United States today many hospitals still have not been modernized to meet the advance in medical science.

The hospital must keep abreast of advances in modern medicine. Today a hospital without a recovery room or an intensive treatment room associated with its operating rooms is not abreast of medical progress and is not providing its patients with the facilities that they should have. The laboratories for clinical pathology vary from those with a few test tubes and beakers to those equipped with all the newer devices developed through research in automation to do great numbers of laboratory tests with greater accuracy and much more rapidity than previously. The new developments in the field of x-ray mean that every hospital must resurvey its roentgenographic equipment to determine whether or not it is giving the most that can be had from this invaluable source of information. Moreover, the competition for personnel, particularly in the field of nursing, means that hospitals everywhere are striving more and more to offer suitable housing, recreation and other facilities to attract young women into nursing.

These requirements place a great burden on the funds available to the hospitals of the United States in providing care for the people. Thirty-five years ago when the great drive was on to socialize medicine in the United States and possibly to bring all hospitals under government control, as is the situation today in Great Britain, the battle was won, at least temporarily, by the development of Blue Cross and Blue Shield insurance. That development encouraged private insurance companies to enter the field competitively. Today about 120 million of the 176 million people in the United States are covered by hospitalization insurance. However, the disturbances prevalent throughout the country indicating some dissatisfaction with our hospitalization insurance system are a warning that constant consideration is necessary to keep our insur-

ance system up to the needs of the institutions and the people that they serve. The premiums must be adequate to cover the costs of hospital care. Most unfortunate is the point of view that carrying hospitalization insurance is some sort of charity instead of a simple economic procedure. As costs rise, the premiums must be increased to meet these costs; otherwise, dissatisfaction is followed by discontinuance of the insurance.

Dr. John C. Haldeman, Assistant Surgeon General in the U. S. Public Health Service administering the hospital construction act, recently pointed out that today the greatest urgency for hospital facilities is in the cities. "Hospital costs have gone up," he said, "out of all proportion to cost-of-living increases. Since 1949 the consumer price index has risen about 22 per cent, while the average cost per patient per day in a general hospital has increased by 94 per cent. Ten years ago the average number of laboratory procedures per patient was four. Now it is 14."

The statistics indicating the vast increase in the birth rate and in population mean that planning should be constant for the necessary increases in beds available in hospitals to meet the rising need.

Apparently, far too many ambulatory patients are sent to the hospital for diagnostic tests and roentgenographic studies which could be made elsewhere if insurance covered such costs. Certainly, physicians would be just as happy if the patient could be ambulatory and still working rather than lying in a hospital bed while the tests were being performed. Surely some means could be found whereby the hospital profession, the medical profession and the insurance agencies could arrive at some agreement to lessen hospital costs by such simple procedures.

Ever since hospitalization insurance came into being, protests have been made against the practice of the medical profession of keeping patients in hospitals longer than they probably should remain. Sometimes this is simply a matter of negligence. Nevertheless, in its total effect it is a tremendous drain on hospitalization facilities and the costs of maintenance. The problem of vacant beds over the week end, with an excessive demand during the first days of the week, has not yet been met, but it could no doubt be solved by proper medical and hospital cooperation.

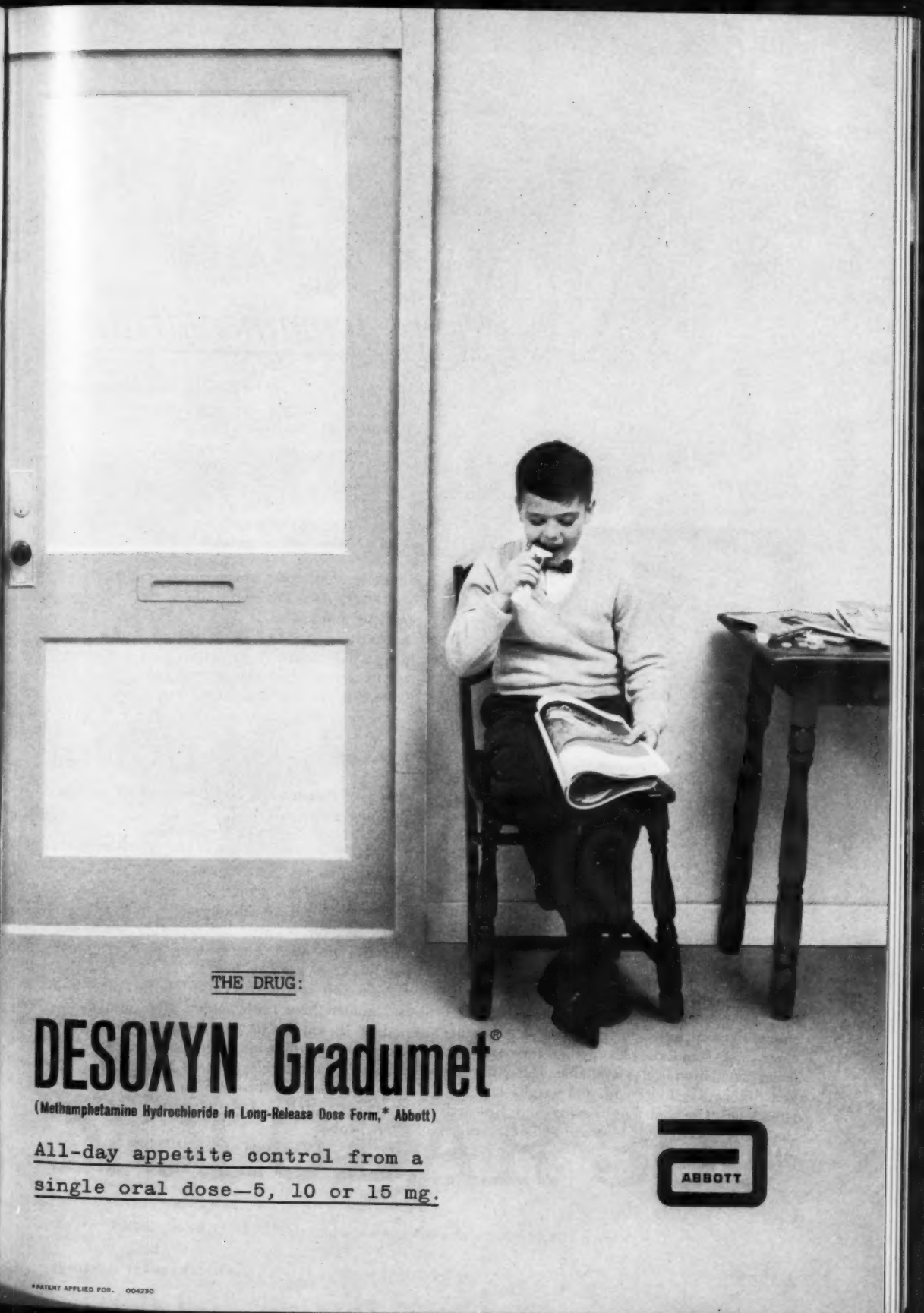
Many of our hospital beds are being occupied by aged persons who really should be in convalescent or nursing homes. The lack of adequate facilities in this field has placed increasing burdens on the hospital.

Finally, any simple analysis of the costs of hospitalization indicates that today the costs of labor represent the primary rise in the costs of hospital care. Various labor organizations are attempting to organize labor in hospitals with the usual emphasis on shorter hours and more pay. This will inevitably still further increase the hospital costs.

What has become of the tradition in medicine of devotion to the sick as a prime motivation for those working in the whole field of medical care? At one time, this extended from the medical profession through the nursing profession, the domestics, the orderlies, the technicians and, in fact, the entire personnel of the hospital. In smaller communities this spirit of service occasionally still prevails, but in most large public hospitals its disappearance is only too obvious. All who care for the sick in any capacity need to be impressed with the dual nature of their occupation; they should consider it not only as a job but also as a devoted service. Such education is in the field of public relations. Some hospitals are beginning to give serious consideration to their public relations both outside the hospital and within its walls.

In medical care every man is his brother's keeper. In hospitals of every type—those supported by religious organizations, by government, by union labor, by industry, and by communities—there must be joint action. In securing the best possible effect there must be mutual consideration of these problems by the boards of directors of hospitals, the professional staff, the nonprofessional workers, and, in fact, by everyone concerned. Only in this way can the immense problems that confront the growth of hospitalization in the United States at this time begin to be met.

MORRIS FISHBEIN



THE DRUG:

DESOXYN Gradumet®

(Methamphetamine Hydrochloride in Long-Release Dose Form,* Abbott)

All-day appetite control from a single oral dose—5, 10 or 15 mg.

ABBOTT

*PATENT APPLIED FOR. 004230

New *for your armamentarium*

Information published in this department is supplied by the manufacturers of the products described.

• THERMAL DETECTOR
(Model 530)

DESCRIPTION: Designed for biophysiologic and therapeutic research and diagnosis, this instrument translator uses various sizes and types of sensing probes. Three probes with impedances of 100, 500 and 1000 ohms are currently available for insertion in body cavities, application to skin surfaces, and other specific uses; other ranges may be adapted as required. Temperature changes as small as 0.025° F. per meter division can be read accurately. Temperatures are indicated on the panel meter and provision is made for use of an external DC meter or recorder. A limit-switch-type relay meter may be used instead of the standard panel meter for automatic temperature control. A standard rack model for rack and panel installation is also available. The unit measures 3⅜ by 4⅛ by 6¾ in. and weighs 4 lb.
PRODUCER: Crescent Engineering and Research Company, Medical Electronics Division, El Monte, Calif.

• BETADINE® AEROSOL SPRAY
(New Product Form)

PURPOSE: Antiseptic and germicidal agent.
COMPOSITION: Povidone-iodine (polyvinylpyrrolidone and iodine).
INDICATIONS FOR USE: Third-degree burns, dermal infections and preoperative and postoperative treatment of dermal ulcers.
PRODUCER: Tailby-Nason Co., New York.

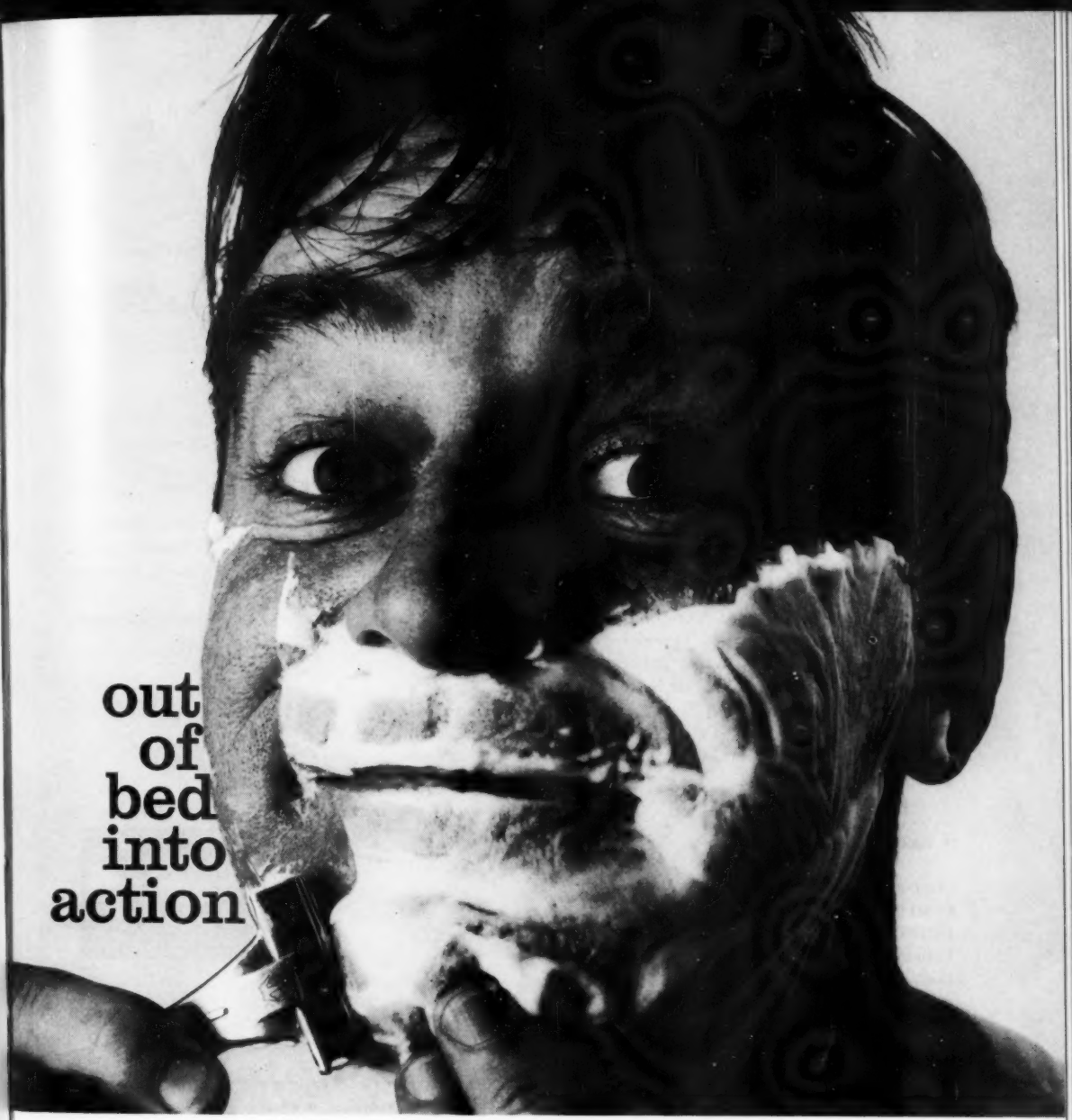
• TRIURATE®

PURPOSE: Prophylaxis and treatment of chronic gout and gouty arthritis.
COMPOSITION: Each tablet contains:

Zoxazolamine (FLEXIN®)	100 mg.
Colchicine	0.5 mg.
Acetaminophen (TYLENOL®)	300 mg.

CAUTION: This drug should not be used in treating acute gout. Nausea, dizziness, drowsiness and urticaria or other allergic-type skin eruptions may occur in some patients.
DOSAGE AND ADMINISTRATION: The average dose is 1 tablet three times a day after meals. The patient should be instructed to drink two full glasses of liquid with each meal and two full glasses between meals.
HOW SUPPLIED: Bottles of 50 and 500.
PRODUCER: McNeil Laboratories, Incorporated, Philadelphia.

(Continued on page A-126)



After a night of deep, refreshing sleep – this is the promise of Noludar 300. One capsule at bedtime acts quickly... eases your patient into sleep without pre-excitement, gives up to 6 or 8 hours of undisturbed sleep without risk of habituation, without toxicity or even minor side effects. Try Noludar 300 for your next patient with a sleep problem. Chances are he'll tell you

"I slept like a log"

NOLUDAR® 300

brand of methyprylon

300-mg capsules

ROCHE LABORATORIES • Division of Hoffmann-La Roche Inc • Nutley 10, New Jersey

• OPTISEAL SERUM VIAL

DESCRIPTION: Featuring a one-piece locked-on plastic closure, this vial provides tamperproof protection for parenterally administered agents. It can be opened safely with one hand by snapping off the plastic knob. The hypodermic needle may be inserted through either rubber plugs or disks. The plastic closure is made by the Lumelite Corporation. The vials are available in nine sizes, ranging from 1 to 25 ml.
PRODUCER: Kimble Glass Company, subsidiary of Owens-Illinois, Toledo.

• TIMOVAN®

PURPOSE: To alleviate anxiety and tension states.
COMPOSITION: Prothipendyl hydrochloride.
CAUTION: Contraindicated in cases of acute alcoholism or barbiturate poisoning.
DOSAGE AND ADMINISTRATION: 1 or 2 tablets three or four times daily.
HOW SUPPLIED: 25 and 50 mg. tablets in bottles of 100 and 1000.
PRODUCER: Ayerst Laboratories, Inc., New York.

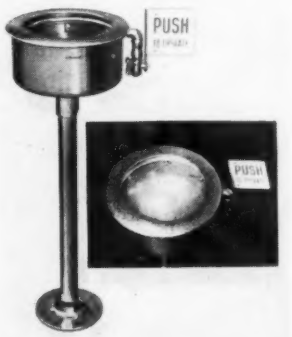
• PENTID®-SULFAS FOR SYRUP

PURPOSE: Antibiotic therapy.
COMPOSITION: Each teaspoonful (5 cc.) contains 200,000 units of potassium penicillin G and 0.5 gm. of triple sulfonamides, buffered with sodium phosphates in a fruit-flavored aqueous suspension.
HOW SUPPLIED: 12-dose bottles, to be reconstituted with 40 cc. of water.
PRODUCER: E. R. Squibb & Sons, division of Olin Mathieson Chemical Corporation, New York.

• CECELL (Model 870)

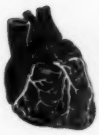
DESCRIPTION: Weighing 700 lb. and measuring 29 by 16 by 45 in., this gamma irradiator provides an average radiation intensity of 50,000 r per hour. The source of radiation is cesium^{137}, which requires less shielding than do other isotopes and has a half-life of about 30 years; it is housed in a stainless steel capsule. The cylindrical irradiation chamber is designed to handle liquids or solids in quantities up to 3¼ in. in diameter and 3¾ in. in length.
PRODUCER: The Victoreen Instrument Company, Cleveland.

• EYE-FACE WASH FOUNTAIN (Model 7955)

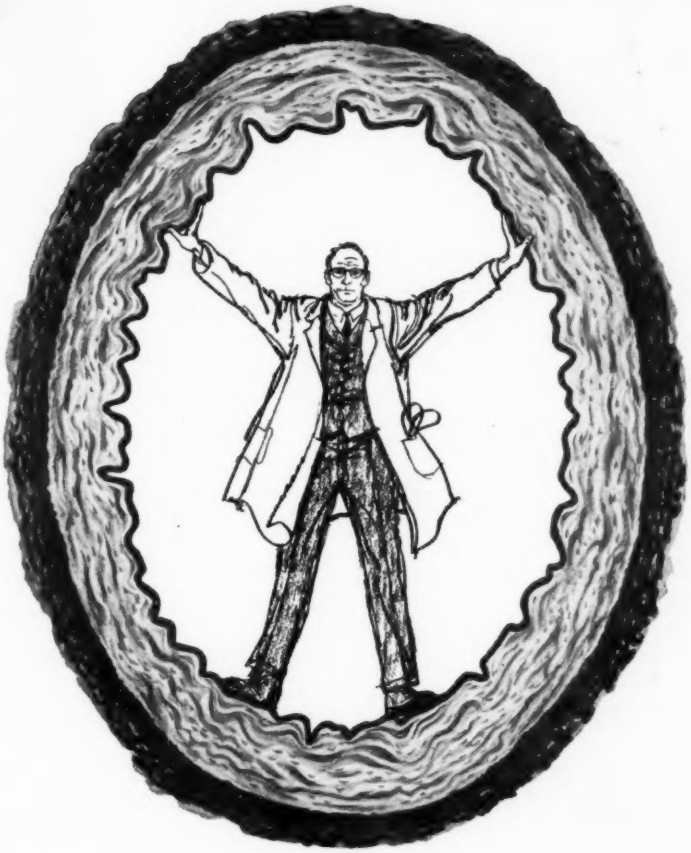


DESCRIPTION: For emergency treatment in accidental contamination of the eyes and face, this unit sprays the facial area with cleansing water from all angles. The large stainless steel bowl contains a 360 degree spray ring with six jets which are activated by a push valve that stays open until manually closed. The jets deliver from 8 to 10 gal. of water per minute on 10 lb. of flow pressure. Both wall and pedestal models of the fountain are available.
PRODUCER: Haws Drinking Faucet Co., Berkeley, Calif.

(Continued on page A-128)



in coronary insufficiency



Metamine® Sustained* helps you dilate the coronaries

METAMINE SUSTAINED (triethanolamine trinitrate biphosphate, 10 mg., in a unique sustained-release tablet) is a potent and exceptionally well tolerated *coronary* vasodilator. Pharmacological studies at McGill University demonstrated that METAMINE "exerts a more prolonged and as good, if not slightly better coronary vasodilator action than nitroglycerin . . . "[1] Work at the Pasteur Institute established that METAMINE exerts considerably less depressor effect than does nitroglycerin.[2] Virtually free from nitrate side effects (nausea, headache, hypotension), METAMINE SUSTAINED protects many patients refractory to other cardiac nitrates,[3] and, given b.i.d., is ideal medication for the patient with coronary insufficiency. Bottles of 50 and 500 tablets. Also: METAMINE, METAMINE WITH BUTABARBITAL, METAMINE WITH BUTABARBITAL SUSTAINED, METAMINE SUSTAINED WITH RESERPINE.

1. Melville, K. I., and Lu, F. C.: Canadian M.A.J., *65*:11, 1951. 2. Bovet, D., and Nitti-Bovet, F.: Arch. Internat. de pharmacodyn. et therap., *83*:367, 1946. 3. Fuller, H. L., and Kassel, L. E.: Antibiotic Med. & Clin. Therapy, *3*:322, 1956.

Thos. Leeming & Co. Inc. New York 17, N. Y.

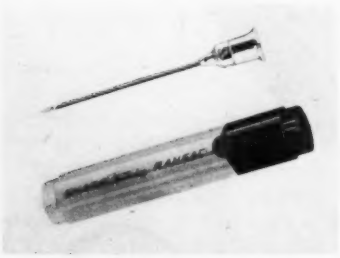
*Patent applied for

• KENALOG IN ORABASE®
(New Product Form)

PURPOSE: Topical therapy for lesions of the oral mucosa.
COMPOSITION: Each gram contains 1 mg. triamcinolone acetonide in emollient dental paste.
HOW SUPPLIED: 5 gm. tubes.
PRODUCER: E. R. Squibb & Sons, division of Olin Mathieson Chemical Corporation, New York.

• PALCILLIN

PURPOSE: To treat infections caused by Gram-positive and Gram-negative organisms.
COMPOSITION: Each 2 cc. contains 400,000 U.S.P. units of crystalline procaine penicillin G in 0.5 gm. streptomycin sulfate solution U.S.P.
INDICATIONS FOR USE: In urinary tract infections, including acute gonococcal infections, and prophylactically in surgery.
DOSAGE AND ADMINISTRATION: 2 cc. once or twice daily, given intramuscularly.
HOW SUPPLIED: 10 cc. multiple-dose vials.
PRODUCER: Philadelphia Ampoule Laboratories, Inc., Philadelphia.



• SHARP-ET HYPODERMIC NEEDLE

DESCRIPTION: Featuring a nontoxic metal hub and a sharp, polished point, this sterile disposable needle is encased in a Sterapac polyethylene cartridge. The heat-sealed hexagonal cartridge fits snugly around the needle hub. When the cartridge is opened, the top is discarded; the lower section may be used as a wrench to engage or disengage the needle. The syringe may be loaded and carried with the needle and cartridge attached, thus assuring sterility. The needle gauge number on the cartridge and the color-coded cartridge top permit easy identification.
PRODUCER: Randall Faichney Corp., Boston.

• DISPOSABLE NIPPLE BAG

DESCRIPTION: Used for covering nipples on nursing bottles, this white paper bag provides space for writing the date, name, nursery and formula. Because it can be autoclaved, it can also serve as a container for sterilizing needles, blades, etc.
PRODUCER: Klean Kan Bag Co., New York.

• INSTANT MIX METAMUCIL®
(New Product Form)

PURPOSE: To treat constipation.
COMPOSITION: A powder containing psyllium hydrophilic mucilloid with citric acid and sodium bicarbonate, which instantly forms an effervescent lemon-flavored liquid when mixed with water.
HOW SUPPLIED: Premeasured dose packets in boxes of 16.
PRODUCER: G. D. Searle & Co., Chicago.

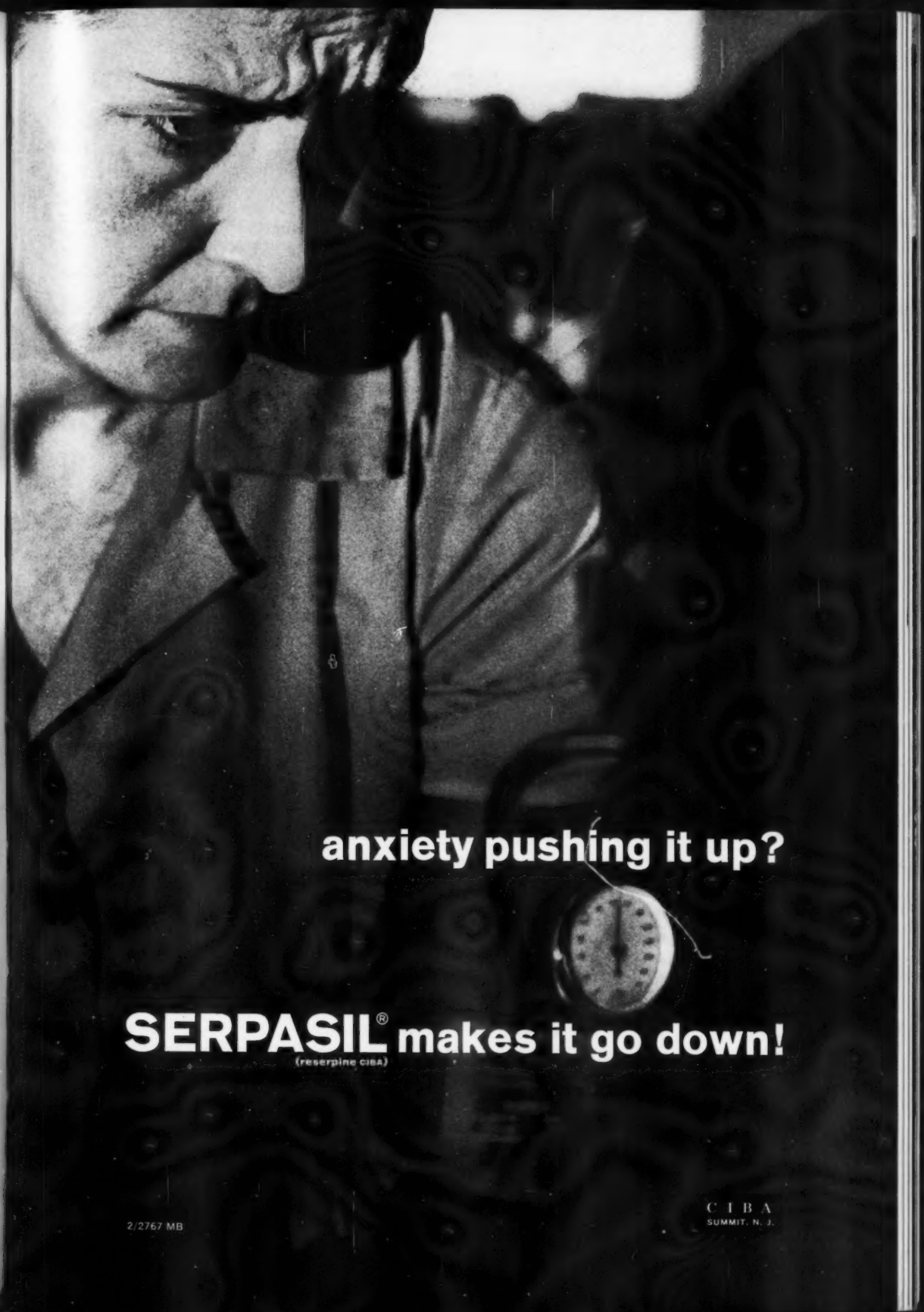
• SYNDECON TABLETS AND POWDER

PURPOSE: Antibiotic therapy.
COMPOSITION: Each tablet or 5 ml. teaspoonful contains:

SYNCILLIN® (potassium alpha-phenoxyethyl penicillin)	62.5 mg.
NALDECON® formula:	
Phenylephrine hydrochloride	2.5 mg.
Phenylpropanolamine hydrochloride	10 mg.
Phenyltoloxamine citrate	3.75 mg.
Chlorpheniramine maleate	1.25 mg.
Acetyl-p-aminophenol	120 mg.

HOW SUPPLIED: Tablets: in bottles of 25. Powder for oral solution: in bottles for reconstitution to 60 ml. with 41 ml. of water.
PRODUCER: Bristol Laboratories, Inc., Syracuse.

(Continued on page A-130)


anxiety pushing it up?
SERPASIL® makes it go down!
(reserpine CIBA)
2/2767 MB
CIBA
SUMMIT, N. J.

• DISPOSABLE EYECUP

DESCRIPTION: Designed to prevent reinfection, this disposable eyecup is made of white, opaque, semirigid plastic. It has a sturdy base to prevent tipping and its curved, smooth edge fits the eye cavity closely.
PRODUCER: Busse Hospital Products, New York.

• MAGNASCALER

DESCRIPTION: A compact radioactivity-measuring device, this unit can collect more than 600,000 counts per minute with an accuracy in excess of 99 per cent. Features include 11 preset time positions for clinical use and 11 preset count positions for preselecting statistical error, a touch bar that resets the instrument automatically, and six electronic decades from which the count can be read directly. The built-in odometer-type timer is accurate within 0.02 of 1 per cent. The Magnascaler can be used with scintillation detectors, Geiger tubes, and proportional counters with preamplifiers; it also can be combined with automatic sample changers and with printers to read out the time and count data. The unit weighs 64 lb. and is 11⅜ in. high, 20⅞ in. wide, and 14 in. deep. The Picker High Voltage Supply is offered as a separate unit.
PRODUCER: Picker X-Ray Corporation, White Plains, N.Y.

• VIDAYLIN®-M (New Formula)

PURPOSE: Nutritional supplement.
COMPOSITION: A homogenized mixture of 11 vitamins, eight minerals and an amino acid in a candy-flavored syrup.
DOSAGE AND ADMINISTRATION: For infants, ½ teaspoon daily; for children, 1 teaspoon daily; for adults, 2 teaspoons daily. The syrup may be given alone or mixed with milk, fruit juice or formula. Therapeutic dosages must be determined individually.
HOW SUPPLIED: 3 and 8 fl. oz. and 1 pt. bottles.
PRODUCER: Abbott Laboratories, North Chicago.

• DISPOSABLE LITTER BAG

DESCRIPTION: Measuring 6 by 3½ by 11 in., this litter bag is made of flame-resistant paper and stands as a square box when opened. A self-stick patch is attached which enables the bag to stick to any surface without damage or marking. Infectious waste may be sealed in by folding the gummed flap forward and sealing it to the face of the bag.
PRODUCER: Klean Kan Bag Co., New York.

• POCKET CARDIAC RESUSCITATOR

DESCRIPTION: Designed for external application, this battery-operated instrument stimulates ventricular function in cardiac arrest. It employs a transistorized circuit and is supplied with a small battery charger. Encased in molded plastic, the instrument measures 4 by 4¼ by 1½ in. and weighs 20 oz.
PRODUCER: Medtronic Inc., Minneapolis.

• DRAMCILLIN®-S

PURPOSE: Antibiotic therapy.
COMPOSITION: Each 5 cc. of powder when reconstituted as a liquid contains 125 mg. potassium phenethicillin.
INDICATIONS FOR USE: Respiratory tract, skin, soft-tissue, surgical, and urinary tract infections; scarlet fever, and puerperal sepsis.
DOSAGE AND ADMINISTRATION: 1 or 2 teaspoonfuls three times daily.
HOW SUPPLIED: Bottles of 30 and 60 cc.
PRODUCER: White Laboratories, Inc., Kenilworth, N. J.

Financial Planning
for the Medical Practitioner

A monthly service dealing with the basic problems of increasing your net income and building personal capital . . . *in the face of today's high tax structure*

prepared by the

J. K. LASSER INSTITUTE

for

Postgraduate Medicine

JUNE 1960

Have You Reviewed Your Will Recently? The Merchants National Bank of Boston points out that intervening changes in family, financial circumstances, tax law, etc. may require revision of your will. Have there been any changes in your family - as a result of births or deaths - since the will was made? You may be disinheriting a child by failure to revise your will after birth of such child.

That is one example why periodic review of your will is necessary. Your will makes a specific bequest to a family member of property which has substantially increased in or lost value. As a result, such family member may get considerably more or considerably less on your death than you originally intended when you first executed your will. Upon retirement, you may change your residence from one state to another. Your will, reflecting probate laws of the state in which you formerly resided, may require revision to facilitate probate under the laws of descent and distribution of the state in which you establish new residence.

Check Settlement Provisions Of Any Life Insurance - when reviewing your will. A recent survey by one of the larger insurance companies revealed that 3 out of 10 insureds who periodically review their will overlook similar check of their insurance policies. One doctor, quite heavily insured, named his wife and his children - with the exception of one - as his beneficiaries. He overlooked his youngest daughter who was born after he purchased insurance. The survey served as a reminder. The daughter now is also named as a beneficiary.

Failure to review settlement provisions of your insurance policies can be costly. One husband named his wife primary beneficiary of his insurance - before the estate marital deduction was made part of the Federal tax law. This deduction allows a taxable estate to be cut up to one-half for property unqualifiedly left to a surviving spouse. Under an insurance option the husband elected, his wife was to receive interest on death proceeds. However, on any interest date, she could demand

payment of insurance proceeds in full. As a matter of course, the insurance companies would pay immediately upon the wife's demand. But under the terms of the policies, the insurance companies could delay payment to her for a period, e.g., up to six months under one insurance contract. The husband thought he had given his wife unqualified rights to his insurance. However, a court held the wife's rights to the insurance proceeds were limited. The insurance proceeds didn't qualify for the estate marital deduction. The husband's taxable estate was increased and a larger estate tax incurred, leaving less for the family.

A Common Disaster Clause Is A Standard Provision - included in most wills and under the settlement terms of insurance policies. It provides for property disposition in case of simultaneous deaths, say of a husband and wife, in a common accident. A standard provision under many insurance policies includes this common disaster clause: "It is agreed that, any provision to the contrary notwithstanding, settlement hereunder shall be withheld until a date 30 days after the death of the insured, and that, for the purpose of making such a settlement, any beneficiary surviving the insured but dying before said date shall be considered as having predeceased the insured."

This common disaster clause can produce probate savings, but it should be used cautiously. Changes in economic circumstances may require its elimination. Consider these examples:

(1) Property holdings of a young couple are not large and are owned by the husband. If the two die in a common disaster, there will be only one estate to probate - that of the husband. There would be no need for a probate of the wife's estate. She doesn't have any separate property, and under this common disaster clause, she doesn't inherit anything from her husband. Probate expenses are thus minimized and more of the husband's estate goes to the children.

(2) Over a period of years, an older husband has amassed sufficient wealth so that he will leave a taxable estate on death. Under such a clause, none of his property would go to his wife. His estate would not benefit from the marital deduction for property left to a surviving spouse. If he left an estate of $300,000, estate taxes would total $70,000 - without benefit of the marital deduction. However, if half of his estate had been left to his wife to secure maximum marital deduction, total estate taxes on probate of the husband's and the wife's estates would run about $40,000.

In the second situation, the will of the husband might be changed to include a common disaster clause which provides that

the wife is presumed to have survived her husband when death results from a common disaster. By leaving part of his estate to his wife, the operation of this clause would require probate of the wife's estate. While that would increase probate expenses, it would mean substantial estate tax savings - about $30,000 in the example.

* * * * *

How Do Your Tax Deductions Compare - with those taken by other taxpayers? Each year, the Treasury Department releases figures on tax deductions taken by taxpayers with varying amounts of income. You don't insure avoidance of an audit of your tax return when your deductions are less than others with similar income. However, if your deductions run higher, chances of an audit are increased. Here are the latest official figures on total deductions (charity, interest, etc.) taken by taxpayers with different incomes.

Income	Total Deductions	Income	Total Deductions
$10,000	$1,700	$22,000	$3,175
12,000	2,000	32,000	4,500
17,000	2,650	65,000	9,100

* * * * *

Do Stocks Of Life Insurance Companies - still have capital gain appeal for the investor? In the past, life companies followed an earnings retention policy. That policy tied to a low rate resulted in a rapid increase in equity values for stockholders. For instance, a $5,000 investment made in Franklin Life on January 1, 1947 appreciated to $150,000 by last year. While life companies will continue an earnings retention policy, they are now taxed at higher rates under a new tax formula. It had been widely predicted that the new tax formula would deprive life companies of their capital appreciation appeal. While tax effect cannot be fully calculated as yet, first year results under the new tax formula are encouraging. Investment potential of life companies may have been downgraded excessively.

Because of increased taxes, General American Life Insurance's investment yield dropped - but only to 3.44% from the previous year's 3.5%. Many other companies suffered less than expected by taking steps to tax protect return on investments. Equitable Life which recently held only $14-million in common stocks began buying equities at the rate of about $40-million a

year after the tax formula was changed. It gets a corporate dividends received credit to tax protect substantially all of the dividends received on stock investment in other U. S. companies. Other life companies increased their holdings of tax-exempt bonds substantially. Initially, at least, it would appear that while tax burden of life companies will be increased, the new tax formula will not adversely affect earnings to the extent originally predicted.

Price-Earnings Ratios Are Useful Guides - in making stock investment. However, such ratios are only guides. A stock selling at a price of 52 which is 13 times current earnings of $4 a share has a low price-earnings ratio, but such ratio doesn't necessarily make such stock a bargain. On the other hand, a stock selling currently at 84 or 21 times current earnings of $4 has a high price-earnings ratio - and may still be a bargain at that price. In using a price-earnings ratio as a guide in making investment, it always is necessary to estimate what earnings the company will be producing in future years.

Stocks which make up the Standard & Poor's industrial market index recently sold at an average price of 16 times 1959 earnings. Over an extended period, those same stocks showed an average growth rate of 5% a year. If you invested in a stock which currently sold at a price 16 times earnings and which had an average growth rate of 5%, your investment would be producing a greater income return by 1965 than another stock currently selling at 13 times earnings which promises little in the way of continued growth. Similarly, you could afford to pay a price 21 times earnings for the typical research-minded company which will grow at an average rate of 10% a year. You would benefit from capital appreciation and greater income return than current investment in the stock offering little growth - even though the latter sold at only 13 times current earnings. Buying a stock with a low price-earnings ratio may be expensive in the long run if the stock offers little in the way of future growth. You sacrifice capital appreciation and future income for a temporarily higher current return on such purchase.

* * * * *

Before Filing Your Tax Return - do you make a last minute check of your arithmetic? The Internal Revenue Service has again pointed out that almost 4 out of every 100 returns filed in 1959 contained errors in addition and subtraction - with 650,000 returns containing mistakes in favor of the Government for an average tax overpayment of $65 a return.

Now available at cost—$1.50—3-ring loose-leaf binder to hold 24 monthly Lasser reports. Made of blue simulated morocco grain leather; non-soil finish with embossed cushion edge. Send check with name and address to POSTGRADUATE MEDICINE, Essex Building, Minneapolis 3, Minnesota.

the ideal:

"by far the most effective drug"

Furadantin®

brand of nitrofurantoin

". . . by far the most effective drug to be employed, and this has been substantiated in practice. It is a drug of low toxicity and, what is more important, bacteria rarely if ever become resistant to it. It can be employed for long periods of time, is bactericidal and does not favor the appearance of monilial infections."[3]

In acute prostatitis: "Antibacterial medication, preferably FURADANTIN (Eaton) 100 mg. 4 times daily is indicated . . ."[4]

In chronic prostatitis: "From clinical observation we have found that more cases of chronic prostatitis respond to FURADANTIN than to any other anti-infection agent."[5]

In benign prostatic hypertrophy (to prevent or treat concomitant infection): "Nitrofurantoin [FURANDANTIN] may be used for protracted periods for the suppression of infection in the urinary tract, even in the presence of probable obstruction . . . it may provide prolonged relief from symptoms and permit better selection of the proper time for surgical or manipulative procedures."[6]

Postoperatively in prostatic surgery: "In conjunction with routine postoperative care, FURADANTIN is frequently used."[7]

FURADANTIN *dosage in prostatitis:* Acute cases—100 mg. tablet q.i.d. with meals and with food or milk on retiring until cured. Chronic cases—100 mg. tablet q.i.d. for 10 to 14 days; depending on response, dosage may then be reduced to 100 or 200 mg. daily for 1 to 3 months.

Supplied: Tablets, 50 and 100 mg., Oral Suspension, 25 mg. per 5 cc. tsp.

References: 1. Campbell, M. F.: Principles of Urology, Philadelphia, W. B. Saunders Co., 1957. 2. Farman, F., and McDonald, D. F.: Brit. J. Urol. **31**:176, 1959. 3. Sanjurjo, L. A.: Med. Clin. N. America **43**:1601, 1959. 4. Barnes, R. W.: Prostatitis. *In* Conn, F.: Current Therapy 1957, Philadelphia, W. B. Saunders Co., 1957. 5. Barnes, R. W., in discussion of Chinn, J., and Bischoff, A. J.: Tr. West. Sect. Am. Urol. Ass. **22**:189, 1955. 6. Jawetz, E.: A.M.A. Arch. Int. M. **100**:549, 1957. 7. Glazier, M., and Lombardo, L. J., Jr.: From the film *Retropubic Prostatovesiculectomy*, Eaton Laboratories, Norwich, N. Y., 1959.

EATON LABORATORIES, NORWICH, NEW YORK

THE MEDICAL *Bookman*

► A TEXTBOOK OF GYNECOLOGY

By Laman A. Gray, M.D., Associate Professor of Obstetrics and Gynecology, University of Louisville School of Medicine, Louisville. 470 pages, illustrated. 1960, Charles C Thomas, Springfield, Illinois. $15.50.

Fulfilling its objective in serving as an outline on which the teacher of gynecology can elaborate, this textbook presents in an interesting and readable fashion points in pathology, diagnosis and treatment. The writing is crisp and fresh, and the text is clearly illustrated with both colored and black-and-white plates. The newness of the illustrations is impressive, and the format makes for easy and rapid perusal. Each section contains its own bibliography, which will introduce the medical student to current literature in gynecology.

Within 16 chapters, beginning with the methods of history taking and the technics of gynecologic examination, the author has included those subjects which the teacher of gynecology may well use as a platform from which to develop his own didactic formulation of the subject. Of particular interest to the practitioner, as well as to the teacher, are the 52 pages devoted to diseases of the ovary. These comprise an outstanding presentation, including not only diagnosis, etiology and treatment but also gross and microscopic plates and, when applicable, the chemotherapeutic approach to eradication.

The concluding chapter best illustrates the completeness of this outstanding text, for here the functional aspects of gynecology and a logical approach to the psychic deviations of female patients are presented. Certainly, this is one of the most complete and informative texts of modern-day gynecology. The author and the editors deserve plaudits for their efforts.

E. A. B.

► EMERGENCIES IN MEDICAL PRACTICE

Edited by C. Allan Birch, M.D., Physician, Chase Farm Hospital, Enfield, England. Ed. 6. 751 pages. 1960, E. & S. Livingstone Ltd., Edinburgh and London. Distributed by The Williams & Wilkins Company, Baltimore. $8.50.

"A medical emergency is any condition or circumstance of a patient which calls for immediate action other than surgery. Just what conditions might be included in this definition are a matter of opinion, and the doctor's list, consisting mostly of absolute emergencies, will be shorter than the patient's, which includes the relative ones." This explanation of a medical emergency by the editor certainly covers the field.

The first chapter concerns the doctor's emergency bag and includes suggestions as to the drugs and appliances that should be carried. This is followed by a short chapter on acute poisonings. The author very wisely has included a discussion on the hazards of medical procedures. Knowledge of these hazards is as important as the knowledge of the emergencies for which some medical procedures are used. Other sections concern the abdominal, gynecologic, cardiovascular, respiratory, nose and throat, renal, neurologic and endocrine emergencies, as well as those re-

(Continued on page A-174)

multiparas need more...

NATALINS® COMPREHENSIVE

Vitamins and minerals

tablets

give them more...more iron, more calcium and more vitamin C

Natalins Comprehensive tablets are formulated to meet the special vitamin-mineral needs of the multipara, whose nutritional stores may have been depleted by successive pregnancies.

Obviously, they are ample for the primigravida as well. Supplying generous amounts of *iron* (40 mg.), *calcium* (250 mg.), and *ascorbic acid* (100 mg.), each Natalins Comprehensive tablet also provides significant quantities of nine other important vitamins and minerals. Recommended dosage is only one tablet daily.

Mead Johnson

Symbol of service in medicine

05560

lating to blood and skin diseases and bites and stings. Also discussed are the emergencies arising in childhood and those occurring in the air, at sea, and in the tropics.

Some chapters are extremely brief, such as the one on emergencies resulting from nuclear and allied radiation, but on the whole the text covers a broad field concisely and eliminates much that the physician already knows. The treatment outlined in some instances is quite meager, and many physicians would resort to more complete volumes for information on most of the medical emergencies discussed in this text.

I. P. F.

► ANATOMY
Regional and Applied

By R. J. Last, M.B., Professor of Applied Anatomy, Royal College of Surgeons of England, London. Ed. 2. 741 pages with 372 illustrations. 1959, Little, Brown & Company, Boston. $15.00.

Written primarily as a review text for students preparing for examinations, this book is particularly directed to those of the Royal College of Surgeons of England. It goes, however, far beyond the mere recitation of important structures and relations that this purpose might imply, for Professor Last is, rightly, primarily concerned with imparting an understanding of anatomy. So successful is he that probably no one can read this book without acquiring some new concepts or new insight into established concepts.

Unfortunately, one must sometimes be a little careful about accepting his statements wholeheartedly. Although it is stated early in the text that there are many aspects of anatomy that are not yet fully understood or agreed on, the implication that opposing concepts will be discussed or at least mentioned is not always borne out. One sometimes has the feeling that the text becomes dogmatic, as if the aim were to present the student with the only acceptable answer to an examination question. For instance, the rotatory action of the iliopsoas and adductor muscles on the thigh, concerning which there are three conflicting views, is treated as if there were no doubt at all that these muscles are internal rotators of the extended thigh. Evidence to the contrary, including some which is recent and some which dates from the time of Duchenne, is ignored. This is certainly the privilege of any writer if he feels such evidence is not pertinent or convincing, but it would seem only proper to have indicated that there are some (misguided?) souls who do not accept the version presented in the text.

The author's categorical statement that the external oblique muscle of the abdomen is not homologous with the external intercostals but rather with certain muscles of the upper limb probably will not be accepted by most anatomists, comparative anatomists and embryologists. At least it was a new concept to this reviewer, who has been a comparative anatomist, experimental embryologist and anatomist, and it does not agree with most current teaching. If there is any convincing evidence on this point, it would seem that the serious student is entitled to it rather than being given an unsupported statement that reads like the recitation of an indubitable fact.

Professor Last's facility for summarizing general principles, a difficult task usually excellently done, occasionally leads him into statements that he obviously does not mean. For instance, in one sentence he correctly states that white fibrous connective tissue elongates only if subjected to prolonged strain, but in the next sentence he asserts that all ligaments composed of white fibrous tissue, with one exception, are so situated that they are *never* (italics mine) subjected to such strain. He is obviously putting himself in the position of denying that ligaments are ever stretched. Furthermore, in trying to make a general point about the nerves to the lower limb, he asserts that nerve L4 does not go to the quadriceps, while in another place he identifies L3 and L4 as being the nerves concerned with extension at the knee.

A possible drawback for American readers may be the use of the British Revision of the Basel anatomic nomenclature, never widely accepted in this country, as standard terminology.

The above criticisms are minor ones and the reader can judge for himself to what extent such things may interfere with his use of the book. The text is regional. The descriptions and the accompanying illustrations are well done; the latter are kept to a minimum, since the text was designed to be used while the actual material was being studied.

In this reviewer's opinion, the book's virtues far outweigh its possible faults. For anyone seeking an additional anatomy text, this will be a useful and often thought-provoking book.

W. H. H.

(Continued on page A-176)

QUIESCENCE

for the medical patient in situational stress

PHENERGAN—available in four convenient forms—helps you cope with situational stress so frequently met in the practice of medicine. Whatever dosage form you choose, PHENERGAN provides these benefits:

quiescence—relief of apprehension; nighttime, perisurgical, obstetrical

control of nausea and vomiting—of pregnancy, motion sickness, or surgical procedures

drug potentiation—of analgesics, barbiturates, anesthetics . . . permitting lower dosages of such agents

allergy control—of allergies amenable to antihistamine therapy

For further information on prescribing and administering PHENERGAN see descriptive literature, available on request.

Wyeth Laboratories Philadelphia 1, Pa.

PHENERGAN®

HYDROCHLORIDE

Promethazine Hydrochloride, Wyeth

INJECTION • TABLETS • SYRUP • SUPPOSITORIES

100 ANNIVERSARY Wyeth®

A Century of Service to Medicine

► TEXTBOOK OF OTOLARYNGOLOGY

By David D. DeWeese, M.D., Clinical Professor of Otolaryngology, University of Oregon Medical School, Portland, and William H. Saunders, M.D., Associate Professor of Otolaryngology, Ohio State University College of Medicine, Columbus. 464 pages with 354 illustrations. 1960, The C. V. Mosby Company, St. Louis. $8.75.

A welcome addition to modern otolaryngology, this textbook is the product of two men who were trained at the University of Michigan, an institution that has made outstanding contributions to this specialty. Each of the authors is now making an important contribution to undergraduate teaching. Because of their experience, they are well qualified to write such a book.

In the preface the authors state, "This textbook is designed primarily for the medical student and general practitioner. Emphasis is on diagnosis and treatment." This purpose has been accomplished in a well-illustrated, thoroughly up-to-date volume.

This book is not an elementary or a complete reference text. It should find an important place as a text for graduate and undergraduate students and as a guide for the general practitioner.

L. R. B.

► RECENT ADVANCES IN CARDIOLOGY

By Terence East, D.M., Physician-in-charge of Cardiological Department, King's College Hospital, and Curtis Bain, D.M., Consulting Physician, Harrogate General Hospital, London, England. Ed. 5. 421 pages with 133 illustrations. 1959, Little, Brown & Company, Boston. $10.00.

It is difficult to summarize recent advances in cardiology without linking them to long-established knowledge of cardiac physiology and pathology. Without excluding that background, the authors have here produced a textbook of cardiology which emphasizes the advances made since their last previous edition was published in 1948. Of necessity, the treatment of some subjects is rather superficial.

The 10 chapters include discussions of congenital cardiac defects; infections of the heart, aorta and pericardial sac; coronary and noncoronary cardiomyopathies; and hypertension, pulmonary heart disease, heart failure and arrhythmias. There are copious reference lists at the chapter ends and after many separate subjects. The chapter on congenital heart disease is preceded by a very useful summary of the embryology of the heart. Recent knowledge of the noncoronary cardiomyopathies is well presented, and in general the separate sections are very adequate summaries.

There are some criticisms. Two chapters are devoted to abnormalities of rhythm but seem to contain little that has not been available for many years in the ordinary textbook of cardiology. Yet they do not include a discussion of paroxysmal atrial tachycardia with block and the relation of this to digitalis and potassium. Bernheim's syndrome is discussed briefly in two places, although most modern cardiologists would deny that this deserves description as an entity. The use of chlorothiazide is discussed in the treatment of heart failure, but its use is not mentioned in the treatment of hypertension.

In spite of these criticisms, this is a very useful book which encompasses rather more than merely the "recent advances" its title suggests.

D. C. C.

► PEDIATRIC DERMATOLOGY

By Henry H. Perlman, M.D., Clinical Professor of Pediatrics, Jefferson Medical College of Philadelphia. 477 pages with 203 illustrations. 1960, The Year Book Publishers, Inc., Chicago. $18.00.

Dr. Perlman has succeeded in editing a text which constitutes an almost complete outline of all the skin diseases encountered in childhood. There is an excellent chapter on pharmacology and prescriptions, printed on blue paper, which makes it easily accessible for reference. The photographs are well done and include many unusual types of skin diseases, including nevoxanthoendothelioma, peculiar nodular types of sporotrichosis, pediculosis of the eyelids, and pyodermic and eczematous eruptions.

This book is highly recommended to both the general practitioner and the specialist in dermatology. The diagnosis and treatment of children's skin diseases is the most difficult task in dermatology, and there has been a great need for a good book on the subject.

J. H. L.

(Continued on page A-178)

Butazolidin®

brand of phenylbutazone

in arthritis and allied disorders

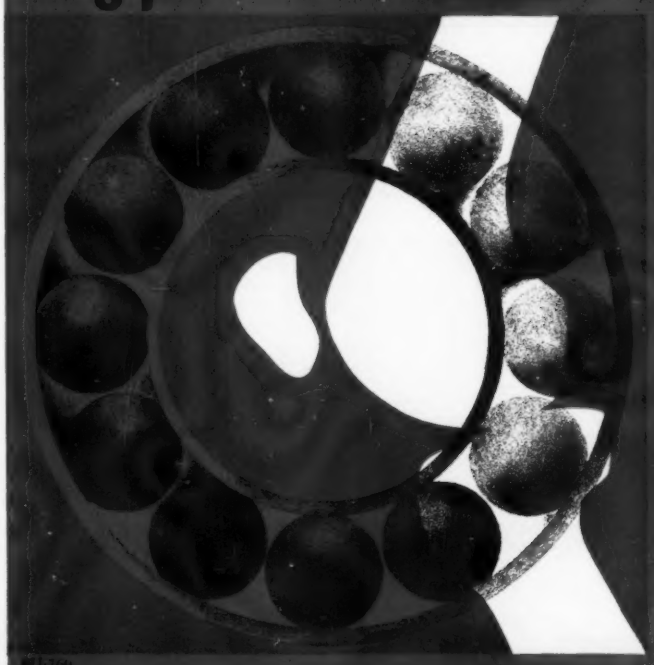
proved by a decade of experience

Ten years of experience in countless cases—more than 1700 published reports—have now established the eminence of Butazolidin among the potent non-hormonal antiarthritic agents.

Repeatedly it has been demonstrated that Butazolidin:
Within 24 to 72 hours produces striking relief of pain.
Within 5 to 10 days affords a marked improvement in mobility and a significant subsidence of inflammation with reduction of swelling and absorption of effusion.

Even when administered over months or years Butazolidin does not provoke tolerance nor produce signs of hormonal imbalance.

Geigy



Butazolidin® (brand of phenylbutazone): Red-coated tablets of 100 mg.
Butazolidin® Alka: Capsules containing Butazolidin® 100 mg.; dried aluminum hydroxide gel 100 mg.; magnesium trisilicate 150 mg.; homatropine methylbromide 1.25 mg.

Geigy, Ardsley, New York

#U-760

► THE YEAR BOOK OF PEDIATRICS (1959-1960)

Edited by Sydney S. Gellis, M.D., Professor and Chairman, Department of Pediatrics, Boston University School of Medicine, Boston. 493 pages with 119 illustrations. 1959, The Year Book Publishers, Inc., Chicago. $8.00.

This annual review of the world's pediatric literature is eagerly awaited and readily consumed by the large following of busy practitioners who cannot find adequate time to devote to their professional reading. All aspects of pediatrics are considered by the editor and are grouped under headings according to organ systems or specialties. The material covers publications from the previous year through the first half of 1959.

The volume is a convenient size; the points are clear, the reviews are concise, and the frequently used illustrations and photographs are of good quality. As usual, the editorial comments are freely interposed and provide some of the best reading in the book. The delightful sense of humor which pervades many of them makes the reading more enjoyable. This book is one from which the reader can obtain much information with a minimum of time at his disposal.

The "Year Book Quiz" provides a stimulus to careful reading of the volume. The current yearbook equals the quality of its predecessors and will command well-earned acclaim from all those who are concerned with the health of children.

S. D. M.

Books received are acknowledged in this department. As space permits, books of principal interest to our readers will be reviewed more extensively. Additional listings will be found on pages 703 and 755 of this issue.

Modern Treatment Yearbook 1960; Yearbook of Diagnosis and Treatment for the General Practitioner. Edited by Sir Cecil Wakeley, F.R.C.S., Consulting Surgeon, King's College Hospital Medical School, London, England, with 34 contributors. Ed. 26. 310 pages, illustrated. 1960, Baillière, Tindall & Cox, Ltd., London. Distributed by The Williams & Wilkins Company, Baltimore. $7.50.

Studies on Vertebrate Neurogenesis. By Santiago Ramón y Cajal, M.D., Universidad Central de España Facultad de Medicina, Madrid, Spain. Translated by Lloyd Guth, M.D., National Institute of Neurological Diseases and Blindness, National Institutes of Health, Bethesda. 432 pages, illustrated. 1960, Charles C Thomas, Springfield, Illinois. $13.50.

Histoplasmosis. Edited by Henry C. Sweany, M.D., Missouri State Sanatorium, Mount Vernon, with 24 contributors. 538 pages, illustrated. 1960, Charles C Thomas, Springfield, Illinois. $14.50.

Dermatologic Medications. By Marguerite Rush Lerner, M.D., Clinical Instructor, Section of Dermatology, and Aaron Bunsen Lerner, M.D., Professor and Head of Section of Dermatology, Yale University School of Medicine, New Haven. Ed. 2. 208 pages, illustrated. 1960, The Year Book Publishers, Inc., Chicago. $6.00.

Atopic Cataract. American Lecture Series. By Emanuel Rosen, M.D., Lecturer in Biomicroscopy, Newark Eye and Ear Infirmary, Newark. 102 pages with 17 illustrations. 1959, Charles C Thomas, Springfield, Illinois. $5.75.

Biochemistry of Human Genetics. Ciba Foundation Symposium. Edited by G. E. W. Wolstenholme, O.B.E. and Cecilia M. O'Connor, B.Sc. 347 pages with 60 illustrations. 1960, Little, Brown & Company, Boston. $9.50.

The Surgical Treatment of Scoliosis. American Lecture Series. By Louis A. Goldstein, M.D., Associate Clinical Professor of Orthopedic Surgery, University of Rochester Medical Center, Rochester, New York. 116 pages with 47 illustrations. 1959, Charles C Thomas, Springfield, Illinois. $6.75.

Henry E. Sigerist on the Sociology of Medicine. Edited by Milton I. Roemer, M.D., Director of Research, Sloan Institute of Hospital Administration, Cornell University Medical College, New York. 397 pages. 1960, MD Publications, Inc., New York. $6.75.

Mitra Operation for Cancer of the Cervix; Extraperitoneal Pelvic Lymphadenectomy and Radical Vaginal Hysterectomy. American Lecture Series. By Subodh Mitra, M.D., Head, Department of Obstetrics and Gynecology, University College of Medicine, Calcutta University, Calcutta, India. 93 pages with 38 illustrations. 1960, Charles C Thomas, Springfield, Illinois. $6.00.

Clinical Management of Behavior Disorders in Children. By Harry Bakwin, M.D., Professor of Clinical Pediatrics, and Ruth Morris Bakwin, M.D., Associate Professor of Clinical Pediatrics, New York University College of Medicine, New York. Ed. 2. 597 pages, illustrated. 1960, W. B. Saunders Company, Philadelphia and London. $11.00.

Atlas of Anatomy and Surgical Approaches in Orthopaedic Surgery—Upper Extremity. By Rodolfo Cosentino, M.D., Research Associate, Department of Orthopedic Surgery, State University of Iowa School of Medicine, Iowa City. Vol. 1. 192 pages, illustrated. 1960, Charles C Thomas, Springfield, Illinois. $10.50.

A Manual of Tropical Medicine. By George W. Hunter, III, Ph.D., Lecturer in Microbiology, College of Medicine and Biological Sciences, University College, University of Florida, Gainesville, William W. Frye, M.D., Dean and Professor of Tropical Medicine, and J. Clyde Swartzwelder, Ph.D., Professor of Medical Parasitology, Louisiana State University School of Medicine, New Orleans, with 33 collaborators. Ed. 3. 892 pages with 323 illustrations, 8 in color. 1960, W. B. Saunders Company, Philadelphia and London. $15.00.

NEW

ORETICYL™

(Oretic® with Harmonyl®)

two effective ingredients compounded into a single tablet:

Oretic. A diuretic-antihypertensive producing maximum diuretic/saluretic effect . . . notably potentiates action of:

Harmonyl. Unique rauwolfia alkaloid fully as effective as reserpine . . . but with lower incidence of side effects such as lethargy, drowsiness and nasal congestion.

three precision dose forms to treat virtually every degree of hypertension:

Oreticyl Forte. Oretic 25 mg., Harmonyl 0.25 mg. Recommended as "initial treatment" form in most cases of moderate to severe hypertension. Usual dose: one t.i.d.

Oreticyl 25. Oretic 25 mg., Harmonyl 0.125 mg.

Oreticyl 50. Oretic 50 mg., Harmonyl 0.125 mg.

Either form for adjustment of dosage once response is seen. Also useful to begin treatment in milder cases.
All 3 in bottles of 100 and 1000.

often gives you a chance to brighten the hypertensive's dreary diet, too . . .

Oretic's pronounced action in eliminating sodium will, in many cases, allow you to adjust diet restrictions so that the patient can enjoy some real salt with his meals.

ORETICYL—TRADEMARK
§ORETIC—HYDROCHLOROTHIAZIDE, ABBOTT
§HARMONYL—DESERPIDINE, ABBOTT

00025

ABBOTT

DR. Pepys' Pages

Personal Diary
and Observations on
Medical Life
by MORRIS FISHBEIN, M.D.

Apr. 1—From Boston by plane to Chicago, reading "The Psychology of Gambling," by Edmund Bergler, and it would have been more fun if his name had been spelled Burglar. Dr. Bergler feels that psychoanalysis can explain why a compulsive gambler will lose all that he has, including his friends and his family, when the compulsion comes upon him. In the evening to dine with Dr. and Mrs. Joseph Calvin who had assembled many of our friends, and enjoyed mathematical contests with Franklin Kahn, Larry Joselit and Roy Grinker.

Apr. 2—By Delta Airlines to Miami and to the Diplomat Hotel, meeting Tom and Terese Rivers, with whom we dined and played bridge.

Apr. 3—With Mistress Pepys to play golf and she made a par and many bogeys and was most happy with the results. In the evening with Dr. Phil Lewin to the Fontainebleau, meeting Lewis Gruber and as his guests observing the great P. Lorillard show honoring their two-hundredth anniversary. Here were Jane Carroll, Jackie Cooper and many fine performers, but best of all was Sam Levenson with his stories of family life and his contrast of the teen-agers of today with the children of our youth.

Apr. 4—All day at the meetings of the Committee on Basic Research, with excellent discussions of immunology and experimental virology. To dine at the Calcutta dining room in the Country Club, where many fine tales were exchanged in a most pleasant evening.

Apr. 5—Again with the Committee on Basic Research, which occupied all day with its numerous considerations.

Apr. 6—This day the Committee on Education of the National Foundation continued its grants for fellowships and for the promotion of the ancillary professions, and this is one of its finest accomplishments in philanthropy. In the afternoon again to play at golf with Mistress Pepys.

Apr. 7—Meeting with the committee that provides medical care, including two clinics on arthritis and two on congenital malformations. In the afternoon returned by plane to Midway Airport.

Apr. 8—Early came Dr. Cowdry from the meeting of the American Society for Cancer Research, and heard of new social problems in China involving the practice of euthanasia and female infanticide. In the afternoon came Sylvia Covet to dine en route homeward from the meeting of the American College of Physicians in San Francisco. We made great plans for future issues of POSTGRADUATE MEDICINE.

Reading now "Through Dooms of Love," by Karl Stern, who is a psychiatrist in Montreal and a gifted novelist. The whole picture of mental institutions becomes apparent in these pages. Here are the variety of psychiatrists, the investigators and the clinicians, and a psychiatric tale of a girl and her father.

Apr. 9—This morning with Mistress Pepys to the grave of our son Junior, who would today have been 44 years old. In the afternoon to see the finals of the basketball professional championships, and later with Samuel Mantel to see the Peace Memorial Home for the Aged, which is about as beautiful a residence as one can find.

Apr. 10—To work at the desk and reading "Ritual in the Dark," by Colin Wilson. His essay under the title "The Outsider" raised a furor as the beginning of the youth "revolt." His novel is, in a word, "mad."

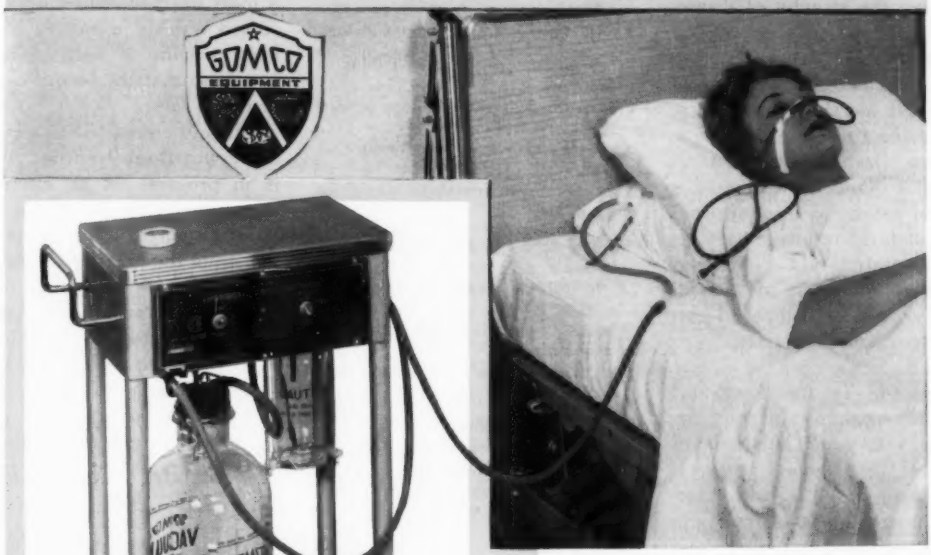
Justin at lunch was full of stories of the famous sinking of the Lady Elgin and of the man on board who founded *The Illustrated London News* with the profits he made from the sale of old Parr's pills, and we wondered if these were named for old Parr on whom William Harvey did a postmortem examination to see if he was really over 170 years old.

Reading a new tale by William Gault, "Death Out of Focus," which shows his mastery of the mystery. Played at gin with Sam Mantel and contributed the cost of his trip. Read also "Waikiki Beachnik," by H. Allen Smith, full of his humor and wise comment but not as instructive as Michener's great novel on the land of the *lei*.

Apr. 11—At the desk conferring with Claire Danziger, who does public relations for the Chicago Heart Association; Peskin, who proposes a new method for universal identification, and Luthin of Abbott Laboratories, who shortly will tour abroad.

(Continued on page A-190)

Its Unfailing Dependability Inspires the Utmost Confidence



Gomco No. 765-A Thermotic® Drainage Pump

Contributing to patient confidence is an important function of physician, nurses and staff. Fine equipment plays its part, too—such as this Gomco No. 765-A Thermotic® Drainage Pump performing gastric lavage.

This economical Gomco stand-mounted unit is entirely automatic. Easily set-up, it operates continuously with quiet, gentle, intermittent action to deliver unvarying suction for all mild drainage. Suction system permits settings at 90 mm. or 120 mm. of mercury. The Gomco Aerovent® valve provides automatic overflow protection.

Investigate the many exclusive advantages of this and other Gomco equipment. A phone call to your Gomco dealer will arrange a demonstration at your convenience.

GOMCO SURGICAL MANUFACTURING CORP.

846-M E. Ferry St., Buffalo 11, N. Y.

Distributed Outside the U. S. A. and Canada by: **INTERNATIONAL GENERAL ELECTRIC COMPANY**
150 East 42nd Street, New York 17, N. Y.

Apr. 12—At noon to speak for the businessmen who raise over $1 million each year for the Chicago Heart Association, and spoke on exercise and rest, emphasizing the atrophy of disuse.

Apr. 13—All day in Dr. Halstead's psychology laboratory at the Albert Merritt Billings Hospital of the University of Chicago. Here Drs. Merriman, Auerbach and others administered a score of psychologic tests to old Pepys and, the results not yet being calculated, old Pepys was pleased at comments of "good," "fine," etc., as he completed particularly the memory tests.

Apr. 14—To the Blackstone Hotel to speak on juvenile delinquency to some hundreds of ladies of the Deborah Society. Ted Remer and his lady entertained many guests, Mrs. Copland presided graciously, and Mrs. Sontag made the introductions. The line that received the greatest amount of applause was, "Professor Koch, who suggested premarital trials in cohabitation in the student magazine of the University of Illinois, was only fired. In my youth he would have been hung, drawn and quartered!" Thereafter to the Peace Memorial Home for the Aged to visit Grandma, who welcomed me warmly and inquired about the quality of the flying en route. Considering Chicago traffic, a helicopter would have been better. In the evening to hear Fritz Reiner conduct Wagner, Saint-Saëns and Dohnányi, and Frank Miller, soon to become associate director of the Minneapolis Symphony, received a great ovation for his solo on the violoncello.

Apr. 15—To lunch with the organization SAVE, which means Service Activities of Volunteer Engineers. This was established by research men from the University of Chicago and the Illinois Bell Telephone Company. Already, new chapters are being developed elsewhere. Dr. Albert Andrews of Presbyterian-St. Luke's described a new roentgenographic technic which gave a claimed 85 per cent positives in cancer of the lung. Dr. Franz Halberg, University of Minnesota Medical School, was searching for a device which would record temperature over a 24 hour period on an ambulatory person. Present projects include: (1) two devices, a miniature stroboscope and a miniature White noise generator, to locate and measure certain fusion levels within the brain and enable the doctor to investigate higher brain functions; (2) two probe devices, a radiation monitoring probe to locate cancerous tissue and a microprobe counter to record the amount of radiation the tissue is absorbing; (3) a small fetal heartbeat monitor to listen to a baby's heartbeat before and during birth; and (4) a mass heart-screening device to record quickly a sample of the heart sounds of each of many people so that the record can be analyzed later.

Already completed is a cumulative heartbeat recorder. Work is in progress on an electronic computer which instantaneously reports changes in air volume to and from the lungs of a newborn as a means of detecting cystic fibrosis; a cytodiagnostic test apparatus for training technicians to identify cells undergoing mitosis; a mechanical calorimeter; and an electronic circuit more sensitive than existing equipment to detect radiation from radioisotopes in brain tumors.

"HIEGH-HO"—SPELLING BY RULE

When I was in school and I learned
how to spell,
They taught me a rule I remember
quite well;
Put "i" before "e"—so I learned when
a brat—
Except after "c," it's as simple as that.

When memory gets muddy, I think in
this vien,
For spelling's a study where sceince
should riegn.
And when deficeint have siezures of
doubt
This rule is sufficeint to straighten
them out.

So why need one labor to reach the
hieght
Or inviegle a nieghbor to set him
aright,
When this anceint rhyme will his
critics inviegh
And never a crime on his consceince
need wiegh.

But while I'm proficeint
At spelling, I've feared
Though the rule is efficeint
The words do look wierd.

* * *

Apr. 17—A pouring rain with great cold marked Easter Sunday. Visited Grandma Mantel at the Peace Memorial Home and dined at Morton's with the Friedells, discussing with young Morris the question of collective behavior of which the growing tendency toward mass marches with banners is an example. And at night saw "The Cherry Orchard," by Chekhov on television while winning three games of "Scrabble."

Apr. 18—Interviews with Ken Arnolt and Silverstein of the National Mental Hospital. On the long-distance talked with Herb Mayes, Ellwood Douglass, Paul Warwick and Bill White, and this means much accomplished with an economy of conversation and an intensity of thought.

Apr. 19—To the Tavern Club for luncheon with Deans LeRoy,

(Continued on page A-193)

Ryan, Young and Bennett and with President Sparling of Roosevelt University and his scientific faculty. Here all of the discussion was on the premedical studies and the admission of medical students, and it was altogether a most enlightening session.

Apr. 20—At noon to confer with prospective secretaries and in the afternoon to sit with Ilza Veith's committee for the entertainment of the American Association for the History of Medicine, which meets here in May 1961. The plans made indicate an interesting and enjoyable time. In the evening with Justin, Barbara and Marjorie and their spouses to Mr. Kelly's to hear the latest humorous sensation Bob Newhart give his telephone conversations with Lincoln and the Wright brothers and similar sketches; particularly amusing was the conversation between a woman taking her driving lesson and her teacher. Thereafter to the Chez Paree to hear a two hour performance by the celebrated Sammy Davis, Jr.

Apr. 21—With Walter Kahoe for one of our enjoyable conferences on books, periodicals, the elections, publishing and travel. The city agog over the White Sox, who display enormous vigor and a competitive disposition. *Time* comments favorably on "The Roguish World of Doctor Brinkley" and the part old Pepys played in it. At noon to the meeting of the Board of Governors of the Chicago Heart Association and sat with Willis Potts and Walter Priest, hearing more of great progress. Then old Pepys dedicated a portrait of S. DeWitt Clough and resolutions were passed to render him tribute, and never were such posthumous honors more merited.

HOWLERS FROM NURSES' EXAMINATIONS IN GREAT BRITAIN

ANATOMY

The heart is the only organ in the body made of heart muscle.

* * *

The mouth is situated in the lower part of the face and is known as the buckled cavity.

* * *

PERSONAL HEALTH

Flies may be shot down while in flight by the aid of DDT bombs.

* * *

If open shoes are worn on duty, the toenails should be kept clean and short as they are on view to all the patients.

* * *

The ear is the organ of earing.

* * *

The common cold is caused by the organism called droplet bacillus.

* * *

If the patient coughs he is very likely to become a little horse.

* * *

Apr. 22—At noon came Mr. Hemans and Dr. Teuscher to talk about the new periodical *Dental Progress*, which will be published by the University of Chicago Press, and we talked with great interest of editing scientific periodicals and the best methods of promotion. Thereafter to visit Dr. Halstead at the University of Chicago and he went over the results of the psychologic studies. Old Pepys found this of great interest, particularly the tests of memory, the definitions and all the other present methods for determining the activity of the brain.

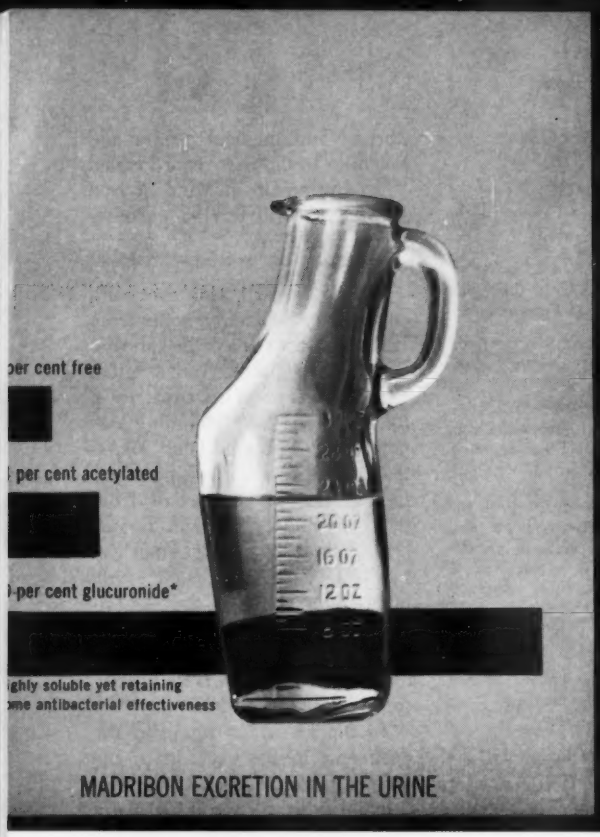
Apr. 23—In the morning working at the correspondence and in the afternoon for a trip to the city, making a variety of purchases. In the evening came Drs. Kirsner and Pearlman to dinner with their ladies, and there was great fun conversing of travel abroad and medical affairs and listening to the new record called "The Button-Down Mind of Bob Newhart," with terrific parodies on modern living.

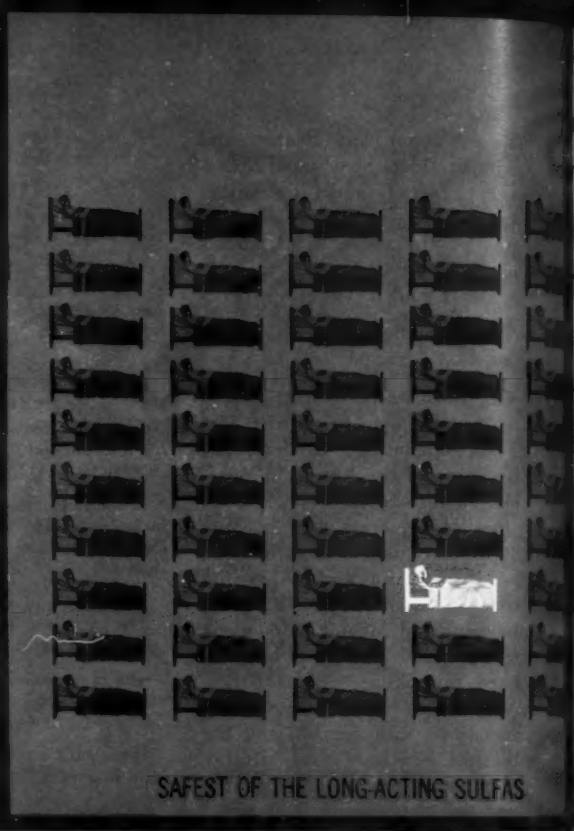
Apr. 25—In the morning came Mary Switzer en route from Washington to speak in Chicago and in Milwaukee. And at noon came a great multitude to a luncheon for her, including our new health commissioner Andelman, our director of welfare Otto Bettag, Lowell Coggeshall from the University, Drs. Blasingame and Talbott from the American Medical Association, and many officials interested in the Department of Health, Education, and Welfare and in the work of rehabilitation, which grows greatly throughout the nation.

In the afternoon again at the desk and in the evening to the Tavern Club to speak to the National Epilepsy League, where a fine trophy and citation were awarded to Mary Switzer, and no one could merit this more. Speaking also were the new officials of the National Epilepsy League, and they announced their new program to buy antiepileptic drugs at a wholesale rate and to distribute them without added profit to those who require them.

Apr. 26—By air to Pittsburgh and then to Wheeling, West Virginia. Here met by Dr. Robert W. W. Phillips and taken to his home, where Mrs. Phillips told me that she was the scrub nurse in the Presbyterian Hospital when I was a patient there in May 1928, but she did not remember me. In the evening to the Oglebay park, where there is a beautiful hotel with golf courses, swimming pools and everything necessary for relaxation. Here came some 200 medi-

(Continued on page A-196)



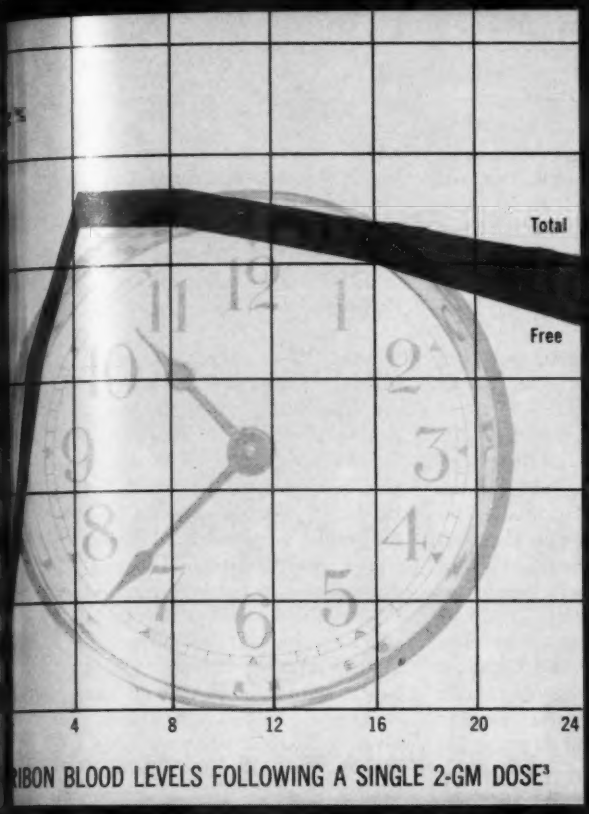


MADRIBON
is modern antibacterial therapy

The safest long-acting sulfonamide, backed by 68 published reports

In tens of thousands of cases on file, Madribon has accumulated a safety record which is significantly superior to that of any other long-acting sulfonamide. One reason: Madribon is metabolized differently – mostly to an extremely soluble glucuronide. The total incidence of side reactions with Madribon lies below 2 per cent; those that have occurred were generally mild and transitory.

Reports and conference papers on Madribon: **1.** R. J. Schnitzer, W. F. DeLorenzo, E. Grunberg and R. Russomanno, *Proc. Soc. Exper. & Med.*, 99:421, 1958. **2.** E. H. Townsend, Jr. and A. Borgstedt, *Antibiotics Annual 1958-1959*, New York, Medical Encyclopedia, Inc., 1959, p. 64. **3.** Boger, *ibid.*, p. 48. **4.** S. Ross, J. R. Puig and E. A. Zaremba, *ibid.*, p. 56. **5.** O. Brandman, C. Oyer and R. Engelberg, *J.M. Soc. New Jersey*, 1959. **6.** L. O. Randall, R. E. Bagdon and R. Engelberg, *Toxicol. & Appl. Pharmacol.*, *1*:28, 1959. **7.** B. Wolach, *Colorado GP*, *1*:4, 1959. **8.** B. Fust and Boehni, *Antibiotic Med. & Clin. Therapy*, 6:(Suppl. 1), 3, 1959. **9.** W. F. DeLorenzo and A. M. Schumacher, *ibid.*, p. 11. **10.** W. F. DeLorenzo and R. Russomanno, *ibid.*, p. 14. **11.** R. J. Schnitzer and W. F. DeLorenzo, *ibid.*, p. 17. **12.** B. A. Koechlin, W. Kern and R. Engelberg, *ibid.*, p. 22. **13.** B. H. Lemmon, C. Flanigan, Jr. and B. R. Jennings, *ibid.*, p. 32. **14.** H. P. Ironson and C. Patel, *ibid.*, p. 40. **15.** W. A. Leff, *ibid.*, p. 44. **16.** J. F. Glenn, J. R. Johnson, J. H. Semans, *ibid.*, p. 49. **17.** J. D. Young, Jr., W. S. Kiser and O. C. Beyer, *ibid.*, p. 53. **18.** T. D. Michael, *ibid.*, p. 57. **19.** J. C. Elia, *ibid.*, p. 61. **20.** S. and A. J. Spiro, *Pediatric Conferences*, *2*:14, 1959. **21.** R. E. Ray, *Case Rep. Child. Mem. Hosp., Chicago*, *17*:4445, 1959. **22.** O. Thalhammer (University Pediatric Clinic, Vienna, Austria), paper presented at the International Congress of Infectious Pathology, Milan, Italy, May 6-10, 1959. **23.** R. Schuppli (Director, versity Dermatological Clinic, Basle, Switzerland), *ibid.* **24.** S. Rummelhardt (First University Surgical Clinic, Vienna, Austria), *ibid.* **25.** M. Rinetti (Institute of Surgical Pathology, University of Parma, Italy), *ibid.* **26.** M. Rentsch (University Pediatric Clinic, Berne, Switzerland), *ibid.* **27.** N. Quattrin (Cardarelli Hospital, Naples, Italy), *ibid.* **28.** E. Picha (First University Gynecological Clinic, Vienna, Austria), *ibid.* **29.** R. Neimeier (University Gynecology Clinic, Switzerland), *ibid.* **30.** G. Moustardier (Faculty of Medicine and St. Andrew's Hospital, Bordeaux, France), *ibid.* **31.** S. T. Madsen (Bergen, Norway) **32.** W. P. Boger, *ibid.* **33.** P. Buenger (Medical Department, Heidberg General Hospital, Langenhorn, Hamburg, Germany), *ibid.* **34.** J. Leng-Levy, *J*



IBON BLOOD LEVELS FOLLOWING A SINGLE 2-GM DOSE[3]

MADRIBON THERAPY IS 'KIND TO THE PURSE'

he most realistic therapy—
ffective, convenient, low in cost

Madribon proves effective against a wide pectrum of bacterial pathogens including, at mes, even those resistant to older antibacterial gents.[13,37,50] Therapeutic blood levels re rapidly attained; easily maintained on the onvenient once-a-day regimen. Prompt sponse plus a low cost-care ratio make Madribon therapy truly economical.

An exclusive development of Roche research, available only from Roche

Supplied: Madribon Tablets: 0.5 Gm, double scored, monogrammed, gold colored—bottles of 30, 100, 250 and 1000. Madribon Suspension: 0.25 Gm/teasp. (5 cc), custard flavored—bottles of 4 oz and 16 oz. Madribon Pediatric Drops: 10-cc plastic container with special tip for dispensing drop dosage—each cc (20 drops) provides 250 mg Madribon.

MADRIBON®—2,4-dimethoxy-6-sulfanilamido-1,3-diazine

ROCHE
LABORATORIES

Division of Hoffmann-La Roche Inc

. *Soc. Exper.* ausse, P. Gibaud and J. Bottin, *J. méd. Bordeaux*, *136*:713, 1959. **35.** B. H. Leming, Jr. and C. Flanigan, Jr., Scientific Exhibit, Annual Meeting of the 59, p. 64. 3. merican Medical Association, Atlantic City, N. J., June 1959. **36.** J. C. Elia, *ibid.* **37.** M. J. Mosely, Jr., *J. Nat. M.A.*, *51*:258, 1959. **38.** H. Schoenfeld and W. *New Jersey,* mmerfeld, *Aerztl. Wchnschr.*, *14*:619, 1959. **39.** H. Ptasnik, *Medizinische*, (31/32), 1437, 1959. **40.** P. Rentchnick and J. Lagier, *Schweiz. med. Wchnschr.*, 8. B. Fust & 894, 1959. **41.** R. E. Bagdon, L. O. Randall and W. A. Leff, *Ann. New York Acad. Sc.*, *82*:(Art. 1), 3, 1959. **42.** W. F. DeLorenzo and R. J. Schnitzer, enzo and R. d., p. 10. **43.** W. P. Boger and J. J. Gavin, *ibid.*, p. 18. **44.** B. H. Leming, Jr. and C. Flanigan, Jr., *ibid.*, p. 31. **45.** T. D. Michael, *ibid.*, p. 40. **46.** S. M. Fine-B. H. Leming d. Z. Kudinoff, H. O. Kendall and V. E. Kvinge, *ibid.*, p. 44. **47.** W. J. Grace, *ibid.*, p. 51. **48.** J. C. Elia, *ibid.*, p. 52. **49.** L. E. Skinner, *ibid.*, p. 57. **50.** G. J. R. Johns Moore, *ibid.*, p. 61. **51.** C. W. Daeschner, *ibid.*, p. 64. **52.** E. H. Townsend, Jr. and A. Borgstedt, *ibid.*, p. 71. **53.** S. Krugman, Discussant, *ibid.*, p. 78. **54.** W. Levy, *ibid.*, p. 80. **55.** M. M. Cahn and E. J. Levy, *ibid.*, p. 84. **56.** M. Sierp and J. W. Draper, *ibid.*, p. 92. **57.** W. S. Kiser, O. C. Beyer and J. D. Young, University Pe d., p. 105. **58.** G. Carroll, Discussant, *ibid.*, p. 110. **59.** H. L. Rosenthal and L. Jud, *J. Lab. & Clin. Med.*, *54*:461, 1959. **60.** A. E. Thill, *Pennsylvania M.J.*, pli (Director 1534, 1959. **61.** Council on Drugs, New and Nonofficial Drugs, *J.A.M.A.*, *171*:1691, 1959. **62.** T. Sakuma, C. W. Daeschner and E. M. Yow, *Am. J.M. Sc.*, H. Rinetti (I 9-92, 1960. **63.** J. W. Faulkner and A. F. Morrison, *J. Urol.*, *83*:181, 1960. **64.** H. Lieb, *Curr. Therap. Res.*, *2*:66, 1960. **65.** G. D. La Veck, F. de la Cruz Quattrin (Ca d J. Kirschvink, *Antibiotic Med. & Clin. Therapy*, *7*:119, 1960. **66.** R. J. Williams, *Antibiotic Med. & Clin. Therapy*, in press. **67.** J. C. Elia, *Mil. Med.*, ology Clinic 5:258, 1960. **68.** N. Mulla, *Obst. & Gynec.*, to be published. **69.** B. Pinck, *J. Urol.*, to be published. **70.** J. C. Elia, *Eye Ear Nose & Throat Month.*, to be en, Norway blished. **71.** H. B. Barner, *Antibiotic Med. & Clin. Therapy*, to be published. **72.** J. P. Cappuccio and E. C. Dobbs, *J. Oral Surg.*, to be published. **73.** A. eng-Levy, J. ittimer, A. J. Simon and M. H. Lepper, *Am. J. M. Sc.*, to be published. **74.** J. C. Elia, *J. Internat. Coll. Surgeons*, *33*:446, 1960.

cos, including the past presidents of the West Virginia State Medical Association, Mr. Lively and his son, Dr. Bogart and many others who had been at Martinsburg. Old Pepys spoke of social security, public relations, medical economics and similar problems. Then to the Wheeling Country Club to meet the ladies and afterward to the home of Dr. Greenhill, who entertained for the society and in particular the anesthetists.

Apr. 27—Early awake and driving with Drs. Perilman and Phillips to Pittsburgh and then by plane to New York. At noon to the Radio City Club for luncheon with Bill White, Bill Lasdon and Max Geffen. Here saw Max Schuster and L. Shimkin and talked of publishing. In the afternoon came Peter Warren to talk of our ventures in "The Voice of Medicine" and *Excerpta Medica.*

Apr. 28—To breakfast came Bill White to discuss editorial functions. Then to confer with Milton Runyon and Richard Whittemore about our new book on the heart and similar projects. Next to discuss problems of research with Dr. John Beckley and Paul Warwick. At noon came Bill Marsden for planning on *World-Wide Abstracts,* and then by plane to Chicago, reading "Its Ugly Head." To dine with the Hertwigs, Karl Meyer, County Commissioner Duffy, Dr. Blaha and the Hoffmans, and played at gin with Duffy and Friedell, who divided the winnings 50-50.

Apr. 29—At noon to dine with Dr. Necheles and his ulcer club composed of executives with peptic ulcer and ulcerative colitis and spoke on "How to grow old disgracefully." To dinner with the Feiwells and found there the eminent attorney Albert Orschel and the former ambassador from Czechoslovakia to France, Osusky, and the conversation having to do with current public affairs and in particular our international relationships was most stimulating and exciting.

Apr. 30—At the desk and at night to attend a fine dinner at the Arts Club, aiding in establishing the Chicago Foundation for Theater Arts. Here was a wonderful play "The Apollo of Bellac," by Jean Giraudoux, and the acting, particularly of Nancy Evans, most exciting. The production was of the best, and old Pepys had special pleasure in watching the play with the eminent Viennese director John Reich, who has charge of the Goodman Theater, and with his lovely lady. Here also were Frank Bering, the Salteils, Mesdames Walter Kraftt and Enloe, and many more.

RICHARD ARMOUR

DOGGING THEIR FOOTSTEPS

Doctors deliver babies
And mailmen deliver mail,
And dogs (very likely with rabies)
Make both of them shudder and pale.

Yes, doctors and mailmen together
Must brave the vociferous beast,
The snarler unfixed to a tether
And ready, it seems, for a feast.

Both men, I should like to assever,
Are faced with a similar fright,
But the mailman is lucky—he never
Must face it in dark of the night!

SURE CURE

By vinegar and honey, mixed,
Now almost every ailment's fixed:
Insomnia, skin rash, bronchitis,
Obesity, and hepatitis,
As well as colds and hypertension
And anything you'd care to mention.

Yes, vinegar and honey solely
Will cure the ailing patient wholly.
It is the best of wonder drugs
With which to rout all sorts of bugs.
At least so says Aunt Sarah, who
Is quite convinced that this is true

Because she heard it from Miss Doakes,
A solemn sort, who never jokes,
Who heard it from a Mrs. Brown
Who shortly afterward left town.

1960 Assembly—Interstate Postgraduate Medical Association—Pittsburgh—October 31-November 3

Volume 27, Number 6 **JUNE 1960**

Postgraduate Medicine

In This Issue

Carcinoma of the Stomach	Samuel F. Marshall	683
Orally Administered Hypoglycemic Agents	George J. Hamwi and Thomas G. Skillman	687
Drugs Effective in Control of Epilepsy	Francis M. Forster	711
Pelvic Pain in Women	William F. Mengert	716
Use of Respiratory Stimulants	John Adriani	723
Scientific Exhibit: Facial Pain	Arnold P. Friedman, Charles A. Carton and Asao Hirano	756
Protein Economy in the Growing Child	L. Emmett Holt, Jr.	783

Complete Contents on Pages A-3, A-4 and A-6

CLINICAL REMISSION IN A "PROBLEM" ARTHRITIC

In disabling rheumatoid arthritis. A 62-year-old printer incapacitated for three years was started on DECADRON, 0.75 mg./day. Has lost no work-time since onset of therapy with DECADRON one year ago. Blood and urine analyses are normal, sedimentation rate dropped from 36 to 7. He is in clinical remission.*

New convenient b.i.d. alternate dosage schedule: the degree and extent of relief provided by DECADRON allows for b.i.d. maintenance dosage in many patients with so-called "chronic" conditions. Acute manifestations should first be brought under control with a t.i.d. or q.i.d. schedule.

Supplied: As 0.75 mg. and 0.5 mg. scored, pentagon-shaped tablets in bottles of 100. Also available as Injection DECADRON Phosphate. Additional information on DECADRON is available to physicians on request. DECADRON is a trademark of Merck & Co., Inc.

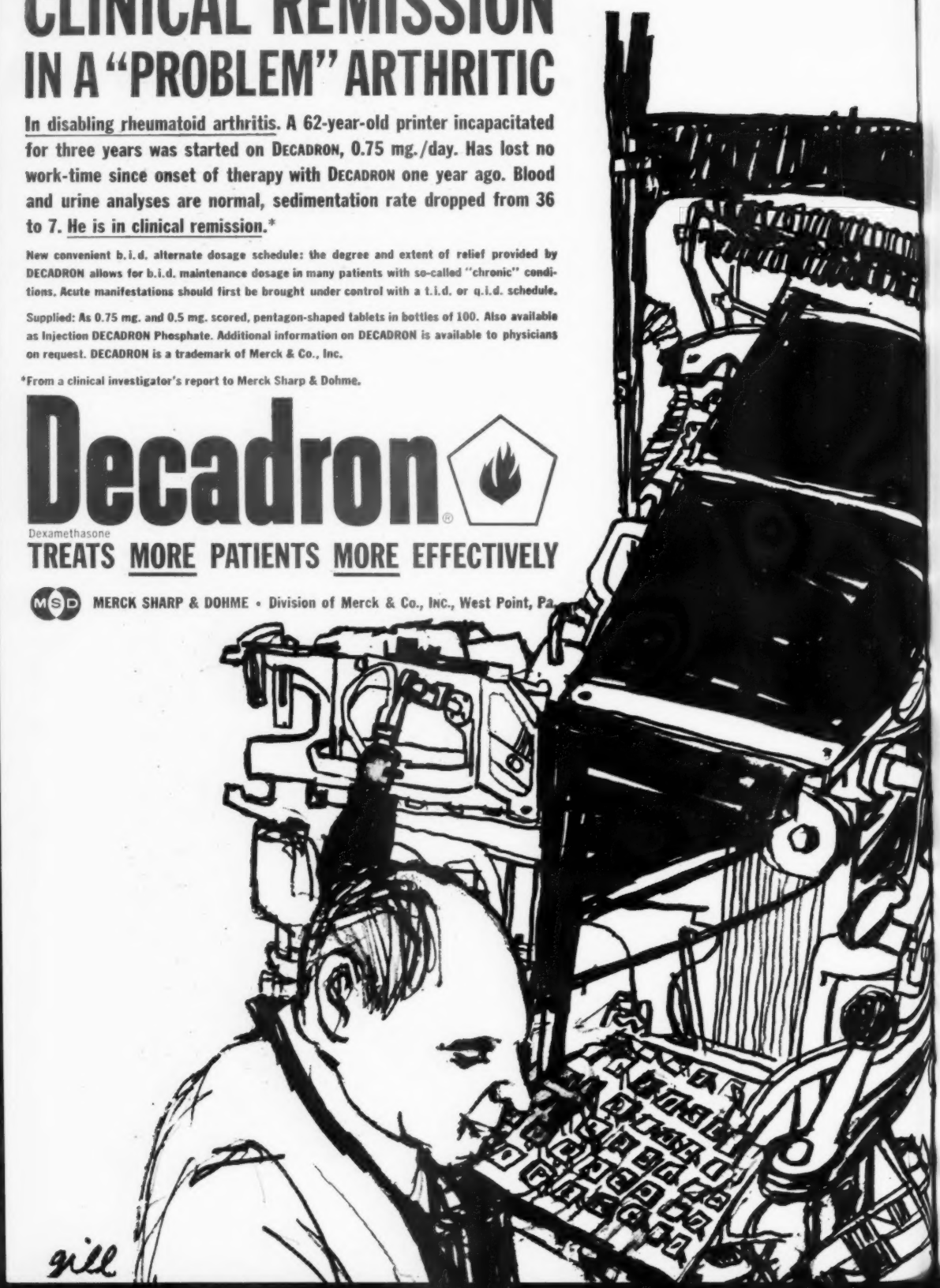
*From a clinical investigator's report to Merck Sharp & Dohme.

Decadron®

Dexamethasone

TREATS MORE PATIENTS MORE EFFECTIVELY

MSD MERCK SHARP & DOHME • Division of Merck & Co., INC., West Point, Pa.



IN EMOTIONALLY PROJECTED SMOOTH-MUSCLE SPASM...

Prompt, Profound Protection...at both ends of the vagus

PRO-BANTHĪNE® *with* DARTAL®

Professional reliance on the therapeutic proficiency of Pro-Banthīne in functional gastrointestinal disorders has made it the most widely prescribed anticholinergic.

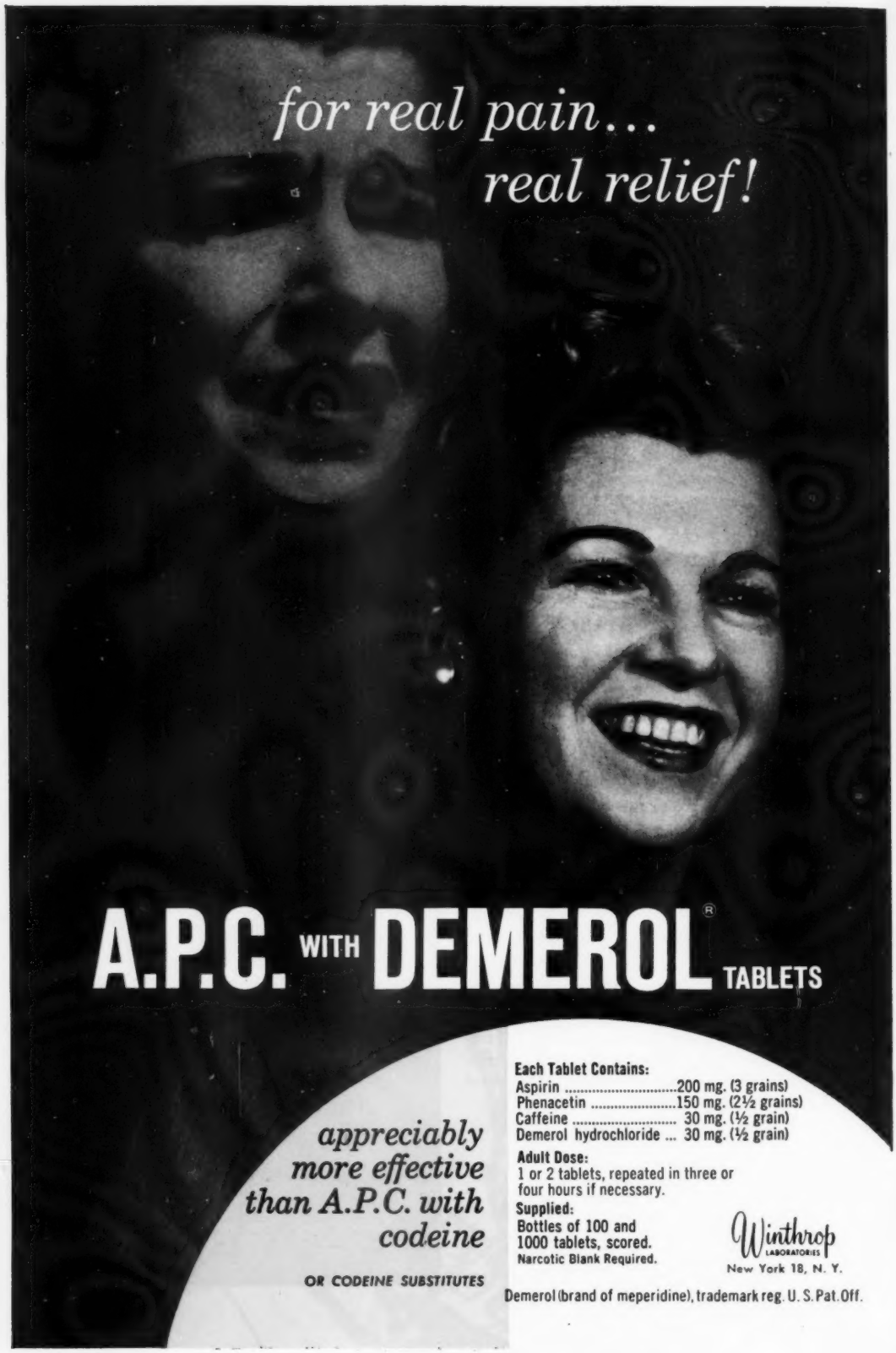
The consistent relief of emotional tensions afforded by Dartal makes this well-tolerated tranquilizer a rational choice to support the antispasmodic action of Pro-Banthīne in emotionally influenced smooth-muscle spasm.

These two reliable agents combined as Pro-Banthīne with Dartal consistently control both disturbed mood and disordered motility when emotional disturbances project themselves through the vagus to provoke such gastrointestinal dysfunctions as gastritis, pylorospasm, peptic ulcer, spastic colon or biliary dyskinesia.

USUAL ADULT DOSAGE:
One tablet three times a day.

SUPPLIED as aqua-colored, compression-coated tablets containing 15 mg. of Pro-Banthīne (brand of propantheline bromide) and 5 mg. of Dartal (brand of thiopropazate dihydrochloride).

G. D. SEARLE & CO.
Chicago 80, Illinois
Research in the Service of Medicine

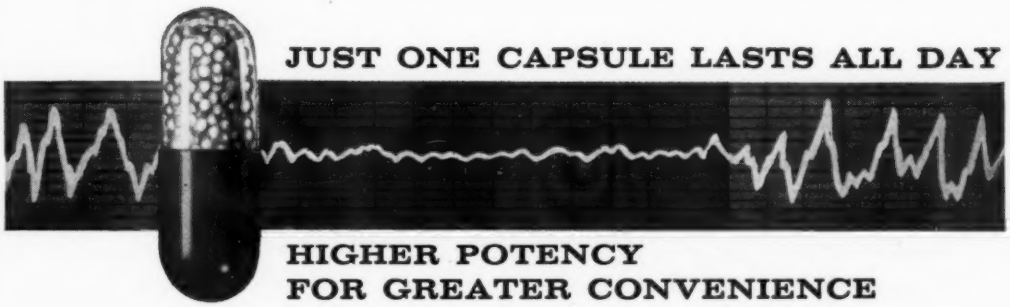

for real pain...
real relief!
A.P.C. WITH DEMEROL® TABLETS
appreciably more effective than A.P.C. with codeine
OR CODEINE SUBSTITUTES
Each Tablet Contains:
Aspirin .....200 mg. (3 grains)
Phenacetin .....150 mg. (2½ grains)
Caffeine ..... 30 mg. (½ grain)
Demerol hydrochloride ... 30 mg. (½ grain)
Adult Dose:
1 or 2 tablets, repeated in three or four hours if necessary.
Supplied:
Bottles of 100 and 1000 tablets, scored.
Narcotic Blank Required.
Winthrop LABORATORIES
New York 18, N. Y.
Demerol (brand of meperidine), trademark reg. U. S. Pat. Off.

NEW AND EXCLUSIVE

FOR SUSTAINED TRANQUILIZATION

MILTOWN® (*meprobamate*) now available
in 400 mg. continuous release capsules as

Meprospan®-400



JUST ONE CAPSULE LASTS ALL DAY

HIGHER POTENCY
FOR GREATER CONVENIENCE

- relieves *both* mental and muscular tension without causing depression
- does not impair mental efficiency, motor control, or normal behavior

Usual dosage: One capsule at breakfast, one capsule with evening meal

Available: *Meprospan-400*, each blue capsule contains 400 mg. Miltown (meprobamate)
Meprospan-200, each yellow capsule contains 200 mg. Miltown (meprobamate)

Both potencies in bottles of 30.

WALLACE LABORATORIES, *New Brunswick, N. J.*

CME-8426

LICENSED BY WISCONSIN ALUMNI RESEARCH FOUNDATION

IN THROMBOPHLEBITIS, CORONARY THROMBOSIS, THROMBO-EMBOLIC PHENOMENA

New

ATHROMBIN®-K

WARFARIN POTASSIUM, PURDUE FREDERICK

TABLETS

THE BEST ORAL ANTICOAGULANT BECOMES EVEN BETTER—AND LESS COSTLY

THE FIRST POTASSIUM SALT OF WARFARIN

- Retains all the therapeutic advantages of earlier Warfarin molecules, but eliminates the sodium ion.
- Less costly for your patients.

ATHROMBIN-K, Warfarin potassium (Purdue Frederick), represents a logical development in anticoagulant therapy—the substitution of potassium for sodium in the Warfarin molecule. With ATHROMBIN-K, the clinical advantages of Warfarin therapy are retained, but with a potassium salt of great purity and stability. Among the established advantages of therapy with Warfarin salts are: **1.** Rapid and predictable action—"...a remarkably easy drug to control, as the response to a given dose can almost invariably be reliably predicted."[1] **2.** Simplified, safer maintenance therapy—"The ability... to provide long periods of stable levels of hypoprothrombinemia for any single patient makes it superior..."[2] **3.** Rapid reversibility with vitamin K_1.

Dosage regimens with 'ATHROMBIN-K' TABLETS are identical and readily interchangeable dose for dose with all Warfarin sodium preparations. For convenience in regulating dosage, 'ATHROMBIN-K' TABLETS are available in 25 mg., 10 mg., 5 mg., and 2 mg. strengths.

1. Toohey, M.: Brit. M. J. No. 5101:892 (Oct. 11) 1958. 2. Fremont, R. E., Jagendorf, B.: J.A.M.A. 165:1381 (Nov. 16) 1957.

PF

The Purdue Frederick Company NEW YORK 14, N. Y. | TORONTO 1, ONTARIO

DEDICATED TO PHYSICIAN AND PATIENT SINCE 1892

© Copyright 1960, The Purdue Frederick Company.

FORTHCOMING FEATURES

IN Postgraduate Medicine

STARTING IN JULY

A Special Series on

INFECTIOUS HEPATITIS

ETIOLOGY AND PREVENTION

ROBERT WARD, M.D., Professor and Chairman, Department of Pediatrics, University of Southern California School of Medicine, Los Angeles

SAUL KRUGMAN, M.D., Associate Professor of Pediatrics, New York University College of Medicine, New York

JOAN P. GILES, M.D., Assistant Professor of Pediatrics, New York University College of Medicine, New York

DIAGNOSIS, INCLUDING SYMPTOMATOLOGY AND LABORATORY TESTS

JOHN R. NEEFE, M.D., Department of Gastroenterology, St. Petersburg Medical Clinic, St. Petersburg, Florida

TREATMENT

MAURICE H. STAUFFER, M.D., Mayo Clinic, Rochester, Minnesota

Senokot
"...a valuable ally in the cure of chronic constipation..."

who said that?

Sir Adolphe Abrahams

O.B.E., M.D., F.R.C.P.,
Consulting Physician, Westminster Hospital,
"Chronic Constipation,"
Practitioner, 170:266, March 1953

natural bowel corrective
Senokot®
TABLETS

BRAND OF STANDARDIZED CONCENTRATE OF TOTAL ACTIVE PRINCIPLES OF CASSIA ACUTIFOLIA PODS, PURDUE FREDERICK

RESTORES
bowel function by reproducing the normal physiologic process of defecation.

•

RESENSITIZES
the specific myenteric plexus (Auerbach's plexus) that mediates the evacuatory response.

•

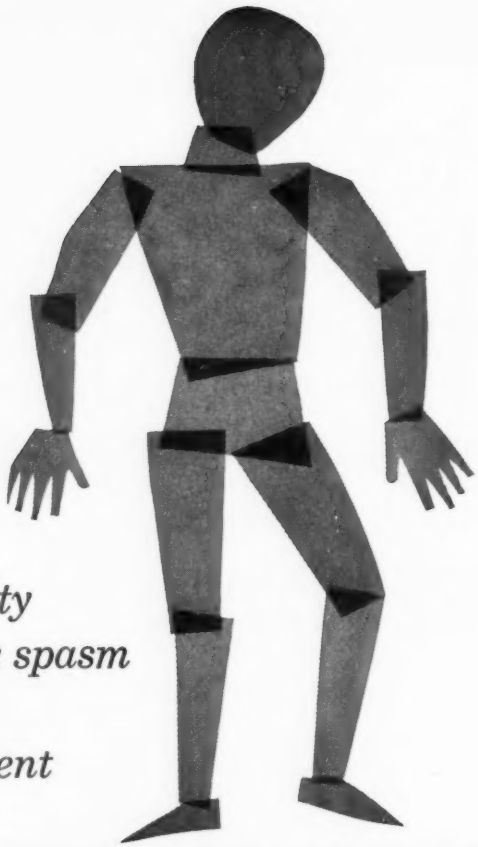
REHABILITATES
the constipated patient by helping to restore normal bowel tone, sensitivity and rhythm.

SUPPLY: Bottles of 100. DOSAGE: Small and easy to swallow. For Adults: 2 to 4 tablets nightly. For Children: 1 to 2 tablets nightly.

The Purdue Frederick Company

DEDICATED TO PHYSICIAN AND PATIENT SINCE 1892
NEW YORK 14, N.Y. | TORONTO 1, ONTARIO

© Copyright 1960, The Purdue Frederick Company



relieves rigidity
and reduces muscle spasm
in the
parkinson patient

PHENOXENE™

a new synthetic compound

"Chlorphenoxamine (Phenoxene) exerts a gentle yet potent action . . . a muscle relaxant action also an energizing and stimulating action, without induction of excitement or agitation. Patients are able to move faster and more freely and with greater strength and longer endurance. It helps to loosen rigid muscles, and it successfully counteracts akinesia, tiredness, and weakness."*

*Doshay, L. J., and Constable, K.: Treatment of Paralysis Agitans with Chlorphenoxamine Hydrochloride, J.A.M.A. *170*:37 (May 2) 1959.

A REPRINT OF THE COMPLETE ARTICLE AND CLINICAL TRIAL SUPPLIES ARE AVAILABLE ON REQUEST.

PITMAN-MOORE COMPANY
DIVISION OF ALLIED LABORATORIES, INC. • INDIANAPOLIS 6, INDIANA

Postgraduate Medicine

OFFICIAL JOURNAL OF THE INTERSTATE POSTGRADUATE MEDICAL ASSOCIATION

Editor-in-Chief
CHARLES W. MAYO, M.D.
Rochester, Minn.

Contributing Editor
MORRIS FISHBEIN, M.D.
Chicago, Ill.

Executive Editor
SYLVIA COVET
Minneapolis, Minn.

EDITORIAL ADVISORY BOARDS

MEDICAL

John F. Briggs, M.D.
ST. PAUL, MINN.

Ray F. Farquharson, M.B.
TORONTO, ONT.

William T. Foulk, M.D.
ROCHESTER, MINN.

J. Roscoe Miller, M.D.
CHICAGO, ILL.

H. Marvin Pollard, M.D.
ANN ARBOR, MICH.

Dwight L. Wilbur, M.D.
SAN FRANCISCO, CALIF.

SURGICAL

Richard B. Cattell, M.D.
BOSTON, MASS.

George W. Crile, Jr., M.D.
CLEVELAND, OHIO

Michael E. DeBakey, M.D.
HOUSTON, TEX.

Howard A. Patterson, M.D.
NEW YORK, N.Y.

Francois Roy, M.D.
QUEBEC, QUE.

I. Ridgeway Trimble, M.D.
BALTIMORE, MD.

CLINICOPATHOLOGIC CONFERENCES

Charles B. Puestow, M.D.
CHICAGO, ILL.

William J. Gillesby, M.D.
CHICAGO, ILL.

FORENSIC MEDICINE

Samuel A. Levinson, M.D.
CHICAGO, ILL.

Milton Helpern, M.D.
NEW YORK, N.Y.

Maier I. Tuchler, M.D.
SAN FRANCISCO, CALIF.

LABORATORY MEDICINE

Ellis S. Benson, M.D.
MINNEAPOLIS, MINN.

NUTRITION

Jean Mayer, PH.D.
BOSTON, MASS.

RADIOLOGY FOR PRACTICING PHYSICIANS

Paul C. Hodges, M.D.
CHICAGO, ILL.

SPECIALTY ADVISORY BOARD

Brian Blades, M.D.	*Thoracic Surgery*	WASHINGTON, D.C.
J. Barrett Brown, M.D.	*Plastic Surgery*	ST. LOUIS, MO.
R. Lee Clark, Jr., M.D.	*Cancer Research*	HOUSTON, TEX.
James L. Dennis, M.D.	*Pediatrics*	OAKLAND, CALIF.
Franklin G. Ebaugh, M.D.	*Psychiatry*	DENVER, COLO.
Edmund B. Flink, M.D.	*Endocrinology*	MINNEAPOLIS, MINN.
Walter Freeman, M.D.	*Neurology*	LOS ALTOS, CALIF.
Chevalier L. Jackson, M.D.	*Laryngology & Broncho-esophagology*	PHILADELPHIA, PA.
Robert A. Kimbrough, Jr., M.D.	*Obstetrics & Gynecology*	PHILADELPHIA, PA.
John H. Lamb, M.D.	*Dermatology & Syphilology*	OKLAHOMA CITY, OKLA.
Julius Lempert, M.D.	*Otology*	NEW YORK, N.Y.
Charles F. McCuskey, M.D.	*Anesthesiology*	LOS ANGELES, CALIF.
Edward B. D. Neuhauser, M.D.	*Radiology*	BOSTON, MASS.
Theodore Rasmussen, M.D.	*Neurologic Surgery*	MONTREAL, P. Q.
Hamilton B. G. Robinson, D.D.S.	*Dentistry*	KANSAS CITY, MO.
Harry L. Rogers, M.D.	*Allergy*	PHILADELPHIA, PA.
Stuart T. Ross, M.D.	*Proctology*	GARDEN CITY, N.Y.
Howard A. Rusk, M.D.	*Rehabilitation*	NEW YORK, N.Y.
Robert D. Schrock, M.D.	*Orthopedic Surgery*	OMAHA, NEBR.
Arthur Purdy Stout, M.D.	*Pathology*	NEW YORK, N.Y.
Gilbert J. Thomas, M.D.	*Urology*	LOS ANGELES, CALIF.
Derrick Vail, M.D.	*Ophthalmology*	CHICAGO, ILL.

GREAT BRITAIN

E. R. Cullinan, F.R.C.P.
LONDON

C. Naunton Morgan, F.R.C.S.
LONDON

R. Guy Pulvertaft, F.R.C.S.
DERBY

AUSTRALIA

Kenneth W. Starr, F.R.C.S.
SYDNEY

Dimetane® Works!

with side effects as few as placebo

—New England J. Med. *261*:478, 1959 (Schiller, I. W. and Lowell, F. C.)

Dimetane works with an effectiveness of 91% in respiratory allergies —NEW YORK J. MED. *59*:3060, 1959 (Fuchs, A. M. and Maurer, M. L.).

In allergic and pruritic dermatoses the effectiveness rate of Dimetane is 94.6% —ANTIBIOTIC MED. & CLIN. THERAPY *6*:275, 1959 (Lubowe, I. I.).

The A. M. A. Council on Drugs characterizes Dimetane as demonstrating "...a high order of antihistaminic effectiveness and a low incidence of side effects." —J.A.M.A. *170*:194, 1959.

for your next allergic patient Rx DIMETANE Extentabs® (12 mg.), Tablets (4 mg.), Elixir (2 mg./5 cc.), new DIMETANE-TEN Injectable (10 mg./cc.) or new DIMETANE-100 Injectable (100 mg./cc.).

Robins

A. H. ROBINS CO., INC., RICHMOND 20, VIRGINIA / ETHICAL PHARMACEUTICALS OF MERIT SINCE 1878

.....and still champion

DESITIN®
OINTMENT

in preventing and healing **diaper rash**

- **blocks** irritation due to urine and excrement
- **fights** ammonia and rash-producing bacteria
- **counters** and clears up chafing, rawness, excoriation

DESITIN OINTMENT the pioneer soothing, protective healing external cod liver oil therapy.

Samples? Please write . . **DESITIN CHEMICAL COMPANY** 812 Branch Ave., Providence 4, R. I.

From Carnation...

a ready-prepared evaporated milk formula

Carnalac is simply Carnation Evaporated Milk with its added Vitamin D, plus carbohydrate. The carbohydrate is natural lactose from the milk, and added maltose-dextrin syrup. Mother adds water in the amount you recommend.

CARNATION EVAPORATED MILK IS THE WORLD'S LEADER FOR INFANT FORMULA FEEDING

"from Contented Cows"

one bridge player has epilepsy...

even his fellow players might not know—if his seizures are adequately controlled with medication Seizures can be adequately controlled in well over 90 per cent of patients, who can then lead normal lives.*

for enhanced control of seizures

DILANTIN® SODIUM KAPSEALS® *time tested—clinically proven in...* ***grand mal and psychomotor seizures...*** DILANTIN Sodium *(diphenylhydantoin sodium, Parke-Davis) is available in several forms including Kapseals of 0.03 Gm. and of 0.1 Gm., bottles of 100 and 1,000.*

other members of THE PARKE-DAVIS FAMILY OF ANTICONVULSANTS ***for grand mal and psychomotor seizures:*** PHELANTIN® Kapseals *(Dilantin 100 mg., phenobarbital 30 mg., desoxyephedrine hydrochloride 2.5 mg.), bottles of 100.* ***for the petit mal triad:*** MILONTIN® *(phensuximide, Parke-Davis) Kapseals, 0.5 Gm., bottles of 100 and 1,000; Suspension, 250 mg. per 4 cc., 16-ounce bottles* • CELONTIN® Kapseals *(methsuximide, Parke-Davis) 0.3 Gm., bottles of 100.*

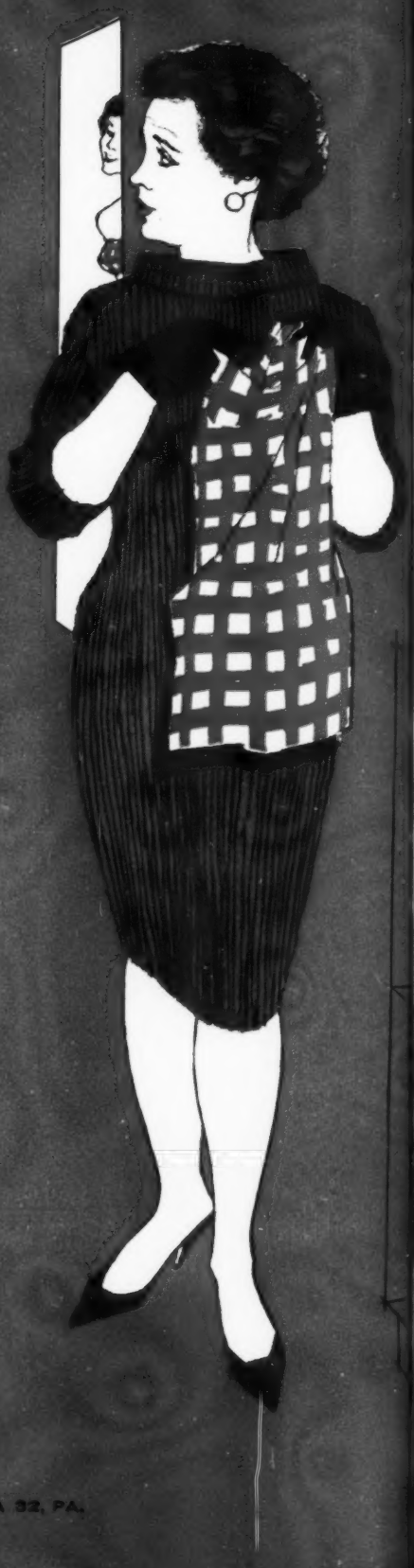
Literature supplying details of dosage and administration available on request.

*Maltby, G. L.: J. Maine M. A. 48:257, 1957.

PARKE, DAVIS & COMPANY • DETROIT 32, MICHIGAN

26180

PARKE-DAVIS



the **"Stylish Stout"**
who'd like a
"Junior Miss"
figure

To help her slim down to "bathing beauty" size—for her health's sake as well as for her social need—

SYNDROX®

methamphetamine hydrochloride

- controls the desire for constant nibbling—suppresses appetite
- takes the mind off food by encouraging activity and a brighter viewpoint
- Dose for appetite suppression: ½ to 1 tab. or tsp. before meals.

SYNDROX TABLETS (5 mg.)
ELIXIR (5 mg. per 5 cc.)

McNEIL

McNEIL LABORATORIES, INC. PHILADELPHIA 32, PA.

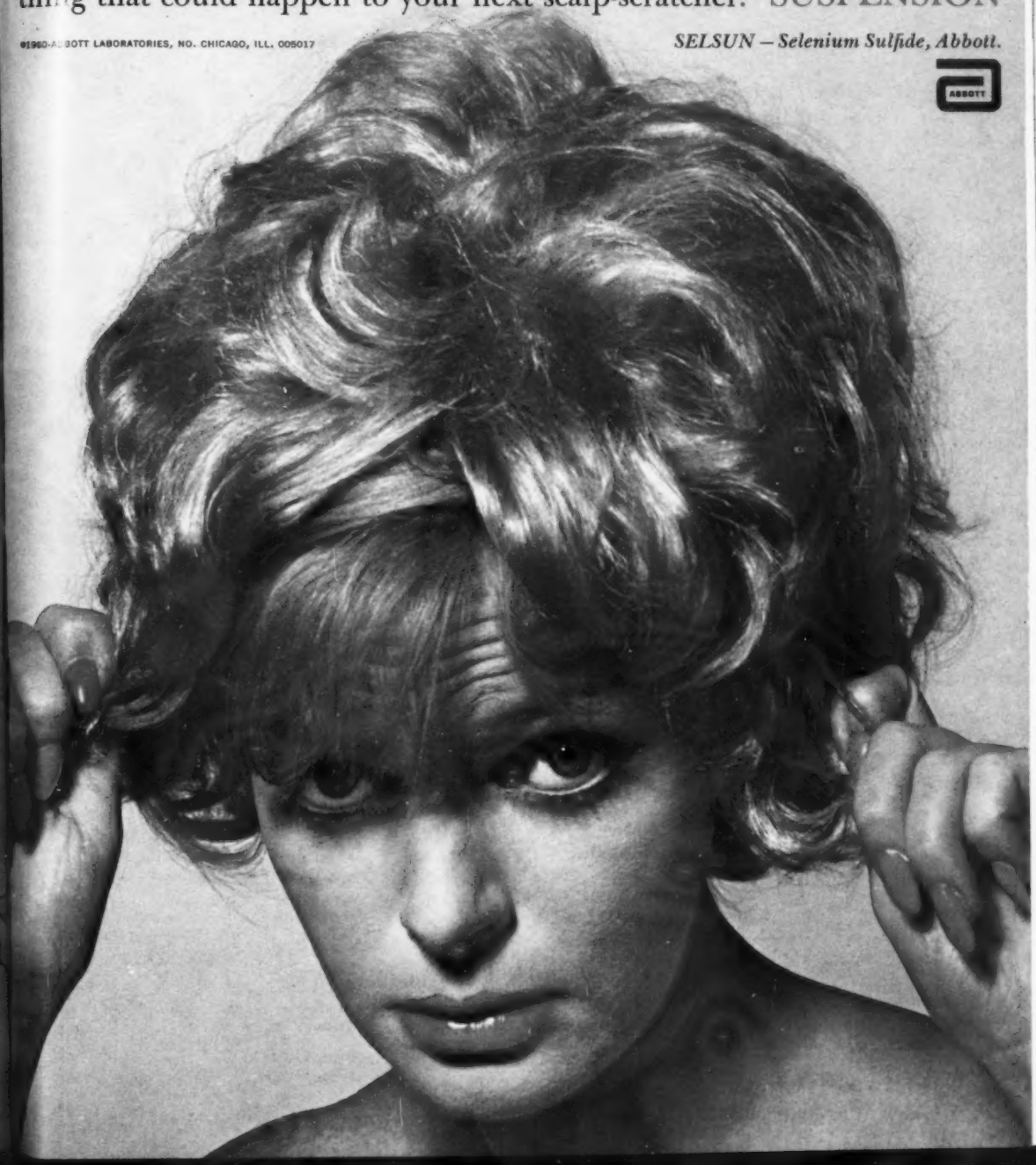
EV N HER DOCTOR DOESN'T KNOW . . . (she has dandruff). The gre t lavender coverup. Too many people take this wig-on-the-head atti-tud toward dandruff . . . if you can't see it, it isn't there. (Besides which, the 've tried all the "sure cures" anyway and yet they're still scratching.) Son eone should tell them there's a medical answer to dandruff control —S lsun.® It could be that an authoritative word from you . . . and a prescription for Selsun . . . would be the best thing that could happen to your next scalp-scratcher.

SELSUN®
AN ETHICAL ANSWER TO A MEDICAL PROBLEM
SUSPENSION

©1960-ABBOTT LABORATORIES, NO. CHICAGO, ILL. 005017

SELSUN — Selenium Sulfide, Abbott.

ABBOTT



ANEMIA OF PREGNANCY

another indication for

filmtab® **Iberol®**

potent antianemia therapy plus the complete B-complex

ABBOTT

2 IBEROL FILMTABS A DAY SUPPLY:

The Right Amount of Iron

Ferrous Sulfate, U.S.P. (Elemental Iron—210 mg.)	1.05 Gm.

Plus the Complete B-Complex

Vitamin B_{12} with Intrinsic Factor Concentrate, 1 U.S.P. Unit (Oral)	
Liver Fraction 2, N.F.	200 mg.
Folic Acid	2 mg.
Thiamine Mononitrate	6 mg.
Riboflavin	6 mg.
Nicotinamide	30 mg.
Pyridoxine Hydrochloride	3 mg.
Calcium Pantothenate	6 mg.

Plus Vitamin C

Ascorbic Acid	150 mg.

® FILMTAB—FILM-SEALED TABLETS, ABBOTT

© 1960—ABBOTT LABORATORIES 005018

90% of anxious, agitated and apathetic office patients calmed without drowsiness and with normal drive restored...

on one or two 0.25 mg. tablets b.i.d.:

This is the pattern of performance for

PERMITIL®

Fluphenazine dihydrochloride

■ In 1164 patients with anxiety and anxiety-induced fatigue or depression, PERMITIL, administered in small daily doses of 0.5 mg. to 1 mg., produced significant improvement in 90%.*

■ PERMITIL is virtually free from side effects at recommended dosage levels.

■ Patients become calm without being drowsy and normal drive is restored.

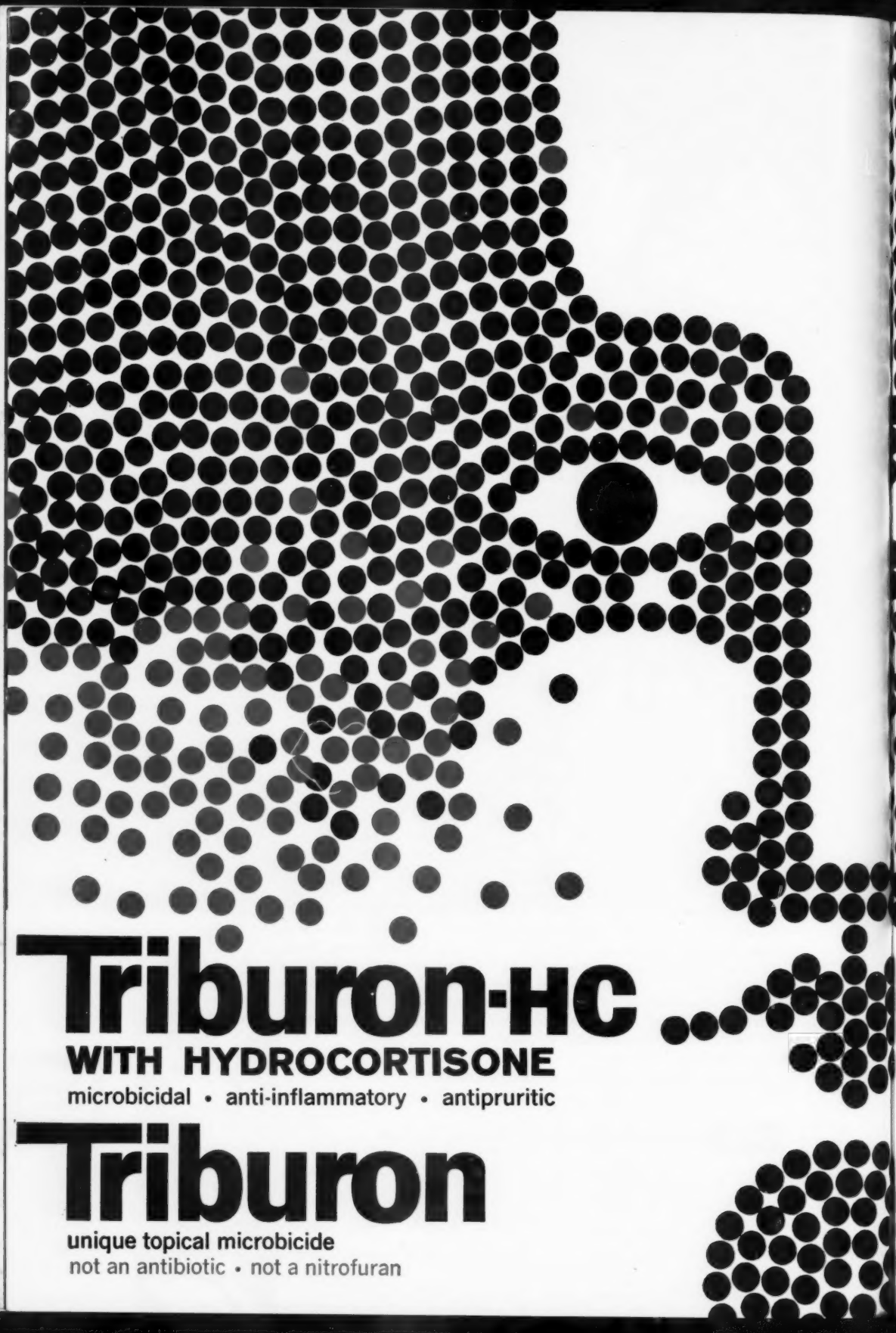
■ Onset of action is rapid; effect is prolonged. ■ PERMITIL does not potentiate barbiturates or non-barbiturate sedatives and can be used with impunity with such agents.

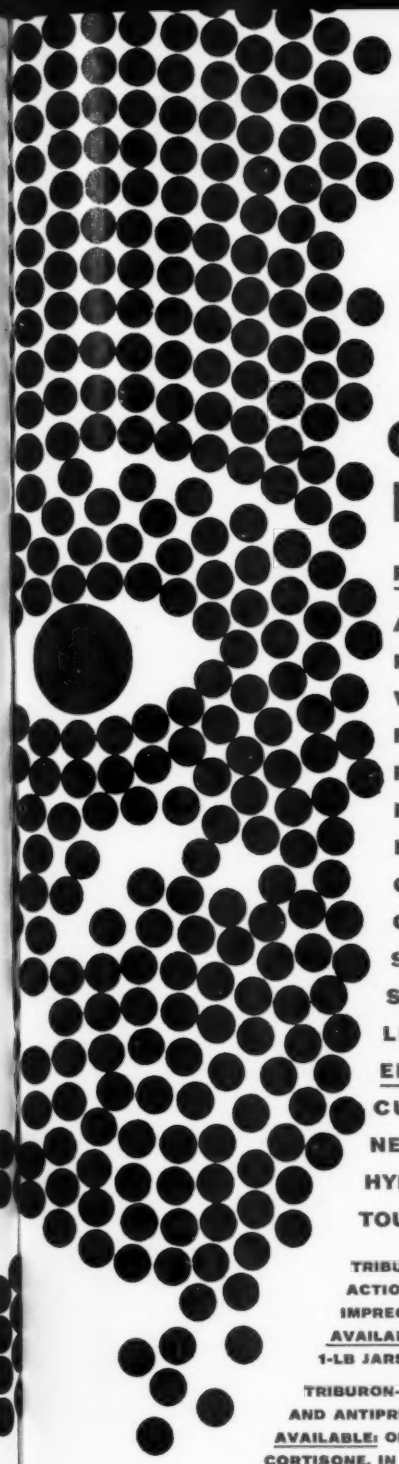
How to Prescribe **PERMITIL:** The lowest dose of PERMITIL that will produce the desired clinical effect should be used. The recommended dose for most adults is one 0.25 mg. tablet twice a day (taken morning and afternoon). Increase to two 0.25 mg. tablets twice a day if required. Total daily dosage in excess of 1 mg. should be employed only in patients with relatively severe symptoms which are uncontrolled at lower dosage. In such patients, the total daily dose may be increased to a maximum of 2 mg., given in divided amounts. Complete information concerning the use of PERMITIL is available on request.

Supplied: Tablets, 0.25 mg., bottles of 50 and 500.

*Recent compilation of case reports received by the Medical Department, White Laboratories, Inc.

White WHITE LABORATORIES, INC., *Kenilworth, New Jersey*


Triburon-HC
WITH HYDROCORTISONE
microbicidal • anti-inflammatory • antipruritic
Triburon
unique topical microbicide
not an antibiotic • not a nitrofuran



CONSISTENT RESPONSE IN SKIN INFECTIONS

REGARDLESS OF VIRULENCE, RESISTANCE, CHRONICITY

A DISTINCTIVE ANTIMICROBIAL, TRIBURON PREVAILS OVER PRIMARY AND SECONDARY INVADERS PROMPTLY, SAFELY, WITH NO SIGNIFICANT LOSS OF ORGANISM SENSITIVITY.[1] TWO FORMS: TRIBURON FOR SKIN AND WOUND INFECTIONS, TRIBURON-HC (WITH HYDROCORTISONE) TO COUNTER ITCHING AND INFLAMMATION AS WELL AS INFECTION. BOTH HAVE ACHIEVED IMPRESSIVE CLINICAL RECORDS: ● EFFECTIVE IN OVER 90% OF PATIENTS[2-5] ● DRAMATIC RESPONSES IN CHRONIC CONDITIONS[4, 6] ● MICROBICIDAL EVEN AGAINST RESISTANT STRAINS OF STAPH. AND STREP.[1, 4] ● VIRTUALLY NON-SENSITIZING AND NONIRRITATING[2-5] ● STAINLESS, ODORLESS, "HIGHLY ACCEPTABLE"[5].

EFFECTIVE THERAPY FOR: IMPETIGO, FOLLICULITIS, FURUNCULOSIS, ECTHYMA, ECZEMA, ACNE, ATOPIC DERMATITIS, NEURODERMATITIS, CONTACT DERMATITIS, STASIS ULCERS, HYDRADENITIS, SEBORRHEIC DERMATITIS, INFECTIOUS ECZEMATOUS DERMATITIS, WOUNDS AND LACERATIONS.

TRIBURON—FOR ALL SKIN AND WOUND INFECTIONS REQUIRING CONSISTENT ANTIBACTERIAL ACTION, AND FOR PREVENTION AND TREATMENT OF POST-BURN INFECTIONS. (TRIBURON-IMPREGNATED DRESSINGS CAN BE AUTOCLAVED.)
AVAILABLE: OINTMENT, CONTAINING 0.1 PER CENT TRIBURON CHLORIDE, IN 1-OZ TUBES AND 1-LB JARS.

TRIBURON-HC—FOR INFLAMMATORY AND ECZEMATOID DERMATOSES WHERE ANTI-INFLAMMATORY AND ANTIPRURITIC BENEFITS AS WELL AS ANTIBACTERIAL EFFECTS ARE REQUIRED.
AVAILABLE: OINTMENT, CONTAINING 0.1 PER CENT TRIBURON CHLORIDE PLUS 0.5 PER CENT HYDROCORTISONE, IN 5-GM AND 20-GM TUBES.

REFERENCES: 1. R. J. SCHNITZER, E. GRUNBERG, W. F. DELORENZO AND R. E. BAGDON, ANTIBIOTICS & CHEMOTHER., 9:267, 1959. 2. R. C. V. ROBINSON, ANN. NEW YORK ACAD. SC., 82:(ART. 1), 144, 1959. 3. E. EDELSON, E. GRUNBERG, A. D. CALABRESE AND T. V. MORTON, IBID., P. 124. 4. P. L. WILLIAMS, IBID., P. 135. 5. F. T. BECKER AND J. L. TUURA, IBID., P. 131. 6. S. M. BLUEFARB, IBID., P. 119.

TRIBURON® CHLORIDE — N,N'-BIS[1-METHYL-3-(2,2,6-TRIMETHYLCYCLOHEXYL) PROPYL]-N,N'-DIMETHYL-1,6-HEXANEDIAMINE BIS (METHOCHLORIDE)

ROCHE LABORATORIES • DIVISION OF HOFFMANN-LA ROCHE INC • NUTLEY 10, N. J.

Armour Pharmaceutical Company Announces a New Systemic Enzyme

Chymoral

I AM PLEASED to inform you of the latest development of our Company's research.

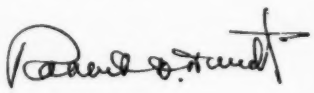
To the expanding field of systemic anti-inflammatory enzymes we are introducing Chymoral. It is a specially coated tablet specifically designed for intestinal absorption. The activity is supplied by a purified concentration which has specific trypsin and chymotrypsin activity in a ratio of approximately six to one.

During past months, clinical investigators have evaluated Chymoral in a wide range of inflammatory conditions. They have reported to us as well as to the medical journals on the therapeutic response, convenience and safety of this oral form.

Patients have responded very well on a Chymoral dosage schedule of 2 tablets q.i.d. and one tablet q.i.d. for maintenance. Important, too, is the fact that where other therapeutic agents were used there were no incompatibilities.

Chymoral is indicated in a wide range of inflammatory conditions to control inflammation, curtail swelling and curb pain.

If you would care to review some of the published reports on Chymoral we shall be happy to send reprints of these papers to you.



Robert A. Hardt
President

1. Beck, C.; Levine, A. J.; Davis, O. F., and Horwitz, B.: Clinical Studies with an Oral Anti-inflammatory Enzyme Preparation. Accepted for publication in Clin. Med. (March) 1960. 2. Billow, B. W.; Cabodevilla, A. M.; Stern, A.; Palm, A.; Robinson, M., and Paley, S. S.: Clinical Experiences with an Oral Anti-Inflammatory Enzyme for Intestinal Absorption. Accepted for publication in Southwestern Med. (May) 1960. 3. Teitel, L. H.; Siegel, S. J.; Tendler, J.; Reiser, P., and Harris, S. B.: Clinical Observations with Chymotrypsin in 306 Patients. Accepted for publication in Indust. Med. (April) 1960. 4. Clinical Reports to the Medical Dept., Armour Pharmaceutical Company, 1959. 5. Reich, W. J., and Nechtow, M. J.: Scientific Exhibit, Chicago Medical Society (March) 1960. 6. Taub, S. J.: Paper presented Annual Meeting, ΠΑΚ Medical Fraternity, Miami, Florida (March) 1960.

© 1960, A. P. Co.

Anturan™

brand of sulfinpyrazone

halting the progress of gout

by potent uricosuric action

By vastly increasing the excretion of uric acid Anturan directly counterbalances the basic metabolic defect in gout.

Clinical experience shows that Anturan: Prevents new tophus formation—causes absorption of pre-existing tophi.[1,2]

Reduces the incidence and severity of acute attacks after the first few weeks of treatment.[3,4]

Relieves interval pain[2,4]—reduces joint swelling[3]—improves mobility.[2]

References:
1. Yü, T. F, Burns, J. J., and Gutman, A. B.: Arth. & Rheumat. *1*:532, 1958. 2. Gutman, A. B., and Yü, T. F: Bull. N. Y. Acad. Med. *34*:287, 1958. 3. Kersley, G. D., Cook, E. R., and Tovey, D. C. J.: Ann. Rheumat. Dis. *17*:326, 1958. 4. Ogryzlo, M. A., and Harrison, J.: Ann. Rheumat. Dis. *16*:425, 1957.

Anturan T.M., brand of sulfinpyrazone: scored tablets of 100 mg. in bottle of 100.
Detailed Literature on Request.

Geigy, Ardsley, New York

Geigy

LN-860

to prevent... or correct... deficiencies THE LEDERLE NUTRITIONAL FORMULAS

Much of the field of nutrition relating to health has fallen into the hands of the faddist and the radio broadcaster.* To protect his patients, the physician should take every opportunity to recommend a program for optimal nutrition.

*Spies, T. D.: J. M. A. Alabama 26:193 (Feb.) 1957.

GEVRAL®

Capsules
Vitamin-Mineral
Supplement

Effective general supplement for the family to ensure optimal nutritional status. Fourteen vitamins, eleven minerals in each dry-filled capsule. Packaged in the decorative dining-table jar. Just 1 capsule daily.

GEVRABON®

Liquid
Vitamins-
Minerals

Unique sherry-flavored liquid supplement particularly favored by senior citizens. Essential vitamins-minerals in attractive decanter bottle (16 oz.). 2 tablespoonfuls daily . . . plain . . . chilled . . . over ice...or as they like it.

FOR COMPLETE FORMULAS SEE 1960 **PDR** Pages 697-698

LEDERLE LABORATORIES
A Division of
AMERICAN CYANAMID COMPANY
Pearl River, New York

Lederle

GEVRINE®

Vitamins-Minerals-Hormones

For the elders — comprehensive nutritional support with androgen and estrogen for proper bone and protein metabolism. Helps reduce or correct tissue atrophy, asthenia, clinical osteoporosis, postmenopausal changes, "aging" mentality. Usually 1 capsule daily. Bottles of 100 and 1,000.

GEVRAL PROTEIN

Vitamin-Mineral-Protein Supplement

High protein (60 per cent) supplement plus 26 vitamins-minerals...to correct or prevent deficiencies, nitrogen imbalance. Ideally suited to those making a general physical "comeback." In ½ lb. jar or 5 lb. can. *New delightful recipes available* on request. Excellent for tube-feeding.

GEVRAL T

Capsules Therapeutic Vitamins and Minerals

High potency formula... broad coverage...for intensive treatment of overt or incipient nutritional failure. 28 factors — including all oil-soluble vitamins, all B-complex, amino acids. Indicated for the convalescent or whenever requirements are abnormally high. In attractive dining-table jar. Usually 1 capsule daily.

"What's the name of that antispasmodic you can prescribe even for patients with concurrent glaucoma?"
"Bentyl gives near-certain results, and it doesn't increase intraocular tension."*
TRADEMARK: BENTYL® (DICYCLOMINE) HYDROCHLORIDE
For fast, sure, safe relief of G.I. spasm and pain, prescribe Bentyl 20 mg. with Phenobarbital. Dosage: 1 tablet t.i.d. *Bibliography on request.
The Wm. S. Merrell Company / New York • Cincinnati • St. Thomas, Ontario
Merrell

against pain

Zactirin®

Provides potent analgesic
and anti-inflammatory benefits
without sedation,
risk of addiction,
tolerance or constipation.

Supplied: Tablets, bottles of 48

Wyeth Laboratories Philadelphia 1, Pa.

100 ANNIVERSARY
Wyeth®

A Century of Service to Medicine

in edema or

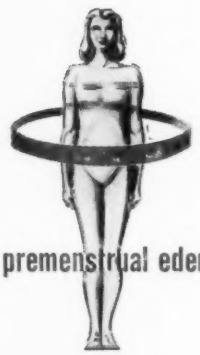
▪ more doctors are prescribing –
▪ more patients are receiving the benefits of –
▪ more clinical evidence exists for –

in congestive failure

"Chlorothiazide was given to 16 patients for a total of 295 patient-treatment days." "Chlorothiazide is a safe, oral diuretic with a clinical effect equal to or greater than a parenteral mercurial." Harvey, S. D. and DeGraff, A. C.: N. Y. State J. Med., **59**:1769, (May 1) 1959.

in hypertension

". . . our program has been one of polypharmacy in which we attempt to deplete body sodium with chlorothiazide. This drug is continued indefinitely as background medication for all antihypertensive drugs." Moyer, J. H.: Am. J. Cardiology, **3**:199, (Feb.) 1959.



in premenstrual edema

"Chlorothiazide is an excellent agent for relief of swelling and breast soreness associated with the premenstrual tension syndrome, since all patients [50] with these complaints were completely relieved." Keyes, J. W. and Berlacher, F. J.: J.A.M.A., **169**:109, (Jan. 10) 1959.

DOSAGE: Edema—One or two 500 mg. tablets DIURIL once or twice a day. Hypertension—One 250 mg. tablet DIURIL twice a day to one 500 mg. tablet DIURIL three times a day.

SUPPLIED: 250 mg. and 500 mg. scored tablets DIURIL (chlorothiazide) in bottles of 100 and 1,000.

DIURIL is a trademark of Merck & Co., INC.

Additional information is available to the physician on request.

hypertension

DIURIL®

(CHLOROTHIAZIDE)

than for all other diuretic-antihypertensives combined!

in edema of pregnancy

"One hundred patients were treated with oral chlorothiazide." "In the presence of clinically detectable edema, the agent was universally effective." "Chlorothiazide is at present the most effective oral diuretic in pregnancy." Landesman, R., Ollstein, R. N. and Quinton, E. J.: N. Y. State J. Med., **59**:66, (Jan. 1) 1959.

in cirrhosis with ascites

"All three of the patients with Laennec's cirrhosis, ascites and edema had a favorable response, with a mean weight loss of 8 lbs., during the five-day treatment period with a slight decrease in edema." Castle, C. N., Conrad, J. K. and Hecht, H. H.: Arch. Int. Med., **103**:415, (March) 1959.

in renal edema

"In a study of 10 patients with the nephrotic syndrome associated with various types of renal disease, orally administered chlorothiazide was a successful, and sometimes dramatic, diuretic agent." Burch, G. E. and White, M. A., Jr.: Arch. Int. Med., **103**:369, (March) 1959.

MSD MERCK SHARP & DOHME
Division of Merck & Co., Inc., Philadelphia 1, Pa.

"Are the xanthines effective in ANGINA PECTORIS?"

(Abstract of the paper with above title)

A favorable response was unequivocally demonstrated with aminophylline when administered intravenously to angina pectoris patients. In sharp contrast the author, noted for his original contributions to cardiovascular research, found oral administration ineffective in all patients tested. This suggested that the failure was correlated with subthreshold theophylline blood-levels obtained with oral administration.

A 20% alcohol-solution of theophylline (Elixophyllin®) has been shown to provide blood levels comparable to those obtained with I.V. administration of aminophylline. This oral preparation and a placebo (identical in appearance, taste and alcoholic content) were tested by the electrocardiographic response obtained and by a double-blind clinical evaluation.

The author reported: "In the light of these findings, conclusions derived from animal experiments which have classed theophylline as a 'malignant' coronary vasodilator must be rejected for man." Elixophyllin administered orally to 30 patients was effective "not only in control of symptoms but in its modifying action on the electrocardiographic response to standard exercise. The efficacy of this preparation is based on the rapid absorption and attainment of high blood levels made possible by the vehicle employed."

(Russek, H. I., Am. J. Med. Sc. Feb., 1960)

CLINICAL REFERENCE DATA ON

ELIXOPHYLLIN®

FORMULA: A hydro-alcoholic solution of theophylline. Each 15 cc. (1 tablespoonful) contains 80 mg. theophylline (equivalent to 100 mg. aminophylline) and 20% ethyl alcohol.

ORAL DOSAGE: First 2 days—doses of 45 cc. t.i.d. (before breakfast, at 3 P.M., and on retiring).
Thereafter—doses of 30 cc. t.i.d. (at same times).

AVAILABLE: Prescription only; bottles of 16 fl. oz. and 1 gallon.

SPECIAL REPRINT: Reprint of Dr. Russek's paper abstracted above on request.

Sherman Laboratories

Detroit 11, Michigan

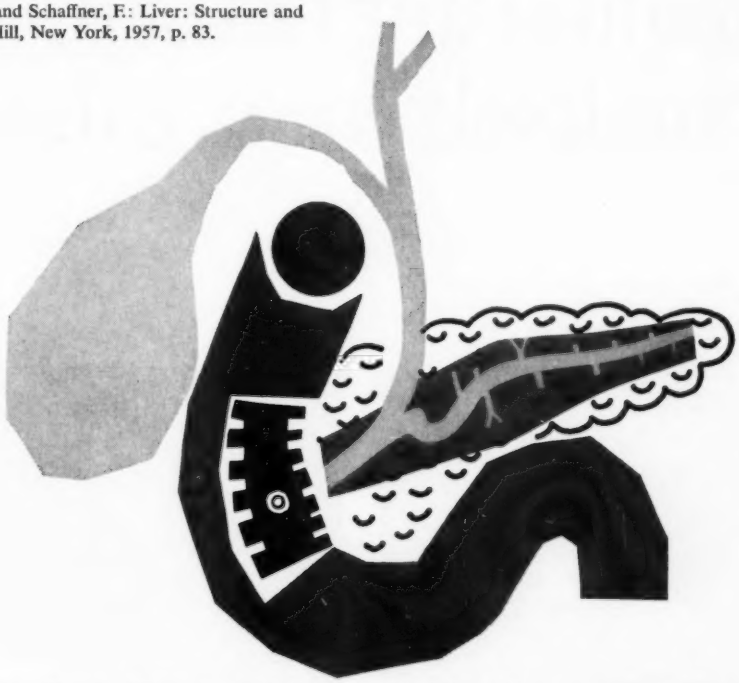
AN AMES CLINIQUICK®

CLINICAL BRIEFS FOR MODERN PRACTICE

how does diet affect the production of bile?

High-protein diets produce the greatest bile flow. Fat is a weaker choleretic than protein, and carbohydrates are without choleretic effect.

Source: Popper, H., and Schaffner, F.: Liver: Structure and Function, McGraw-Hill, New York, 1957, p. 83.



when thin, free-flowing bile is desired... DECHOLIN®

(dehydrocholic acid, AMES)

in biliary infection—"...a copious thin bile facilitates the flushing of the ducts."*

in postoperative management—"After relief of biliary obstruction, acceleration of bile formation, for which administration of bile acids has been suggested, may be desirable."*

Available: DECHOLIN tablets: (dehydrocholic acid, AMES) 3¾ gr. (250 mg.). Bottles of 100, 500, and 1,000; drums of 5,000.

and when spasmolysis is also needed...

DECHOLIN® WITH BELLADONNA

(dehydrocholic acid with belladonna, AMES)

for functional distress of the gastrointestinal tract—especially in geriatrics

Available: DECHOLIN/Belladonna tablets: DECHOLIN (dehydrocholic acid, AMES), 3¾ gr. (250 mg.), and extract of belladonna ⅙ gr. (10 mg.). Bottles of 100 and 500.

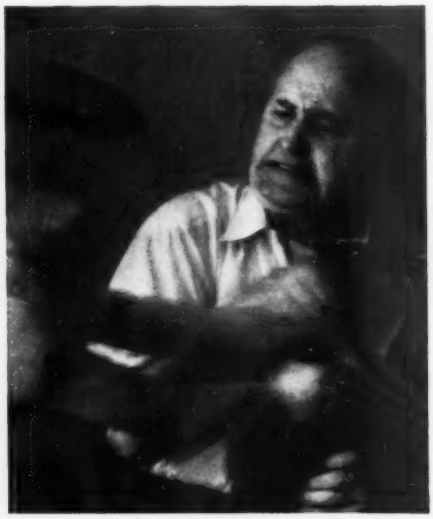
*Popper, H., and Schaffner, F.: *op. cit.*, p. 84.

84660

AMES
COMPANY, INC
Elkhart • Indiana
Toronto • Canada

announcing "Timovan"®
Brand of Prothipendyl hydrochloride

completely new calmative



for the temperamental
older patient

for the emotional
teen-ager

6024

"Timovan"® notably in geriatrics and adolescents

Brand of Prothipendyl hydrochloride

Specifically developed for active patients in need of calming without the "slow-down" of sedatives or the hazards of many tranquilizers. "TIMOVAN" offers a new range of safety and effectiveness in the relief of tension in the ambulatory patient, notably the adolescent and the geriatric. Particularly valuable in conditions in which excessive emotional response complicates therapy, as in dermatoses and allergies.[1-4]

- Reduces excessive response to irritating stimuli.
- Stabilizes the autonomic nervous system.
- Nonhypnotic, yet improves sleep pattern.
- No sensitivity reactions or toxicity reported.
- Has not given rise to drug tolerance even on prolonged use.
- Nonaddictive.
- Preferred to barbiturates.

DOSAGE: One or two tablets three or four times daily. Depending on age of patient and severity of symptoms, dosages ranging from 100 mg. to 400 mg. daily (in divided doses) have been used effectively and safely.

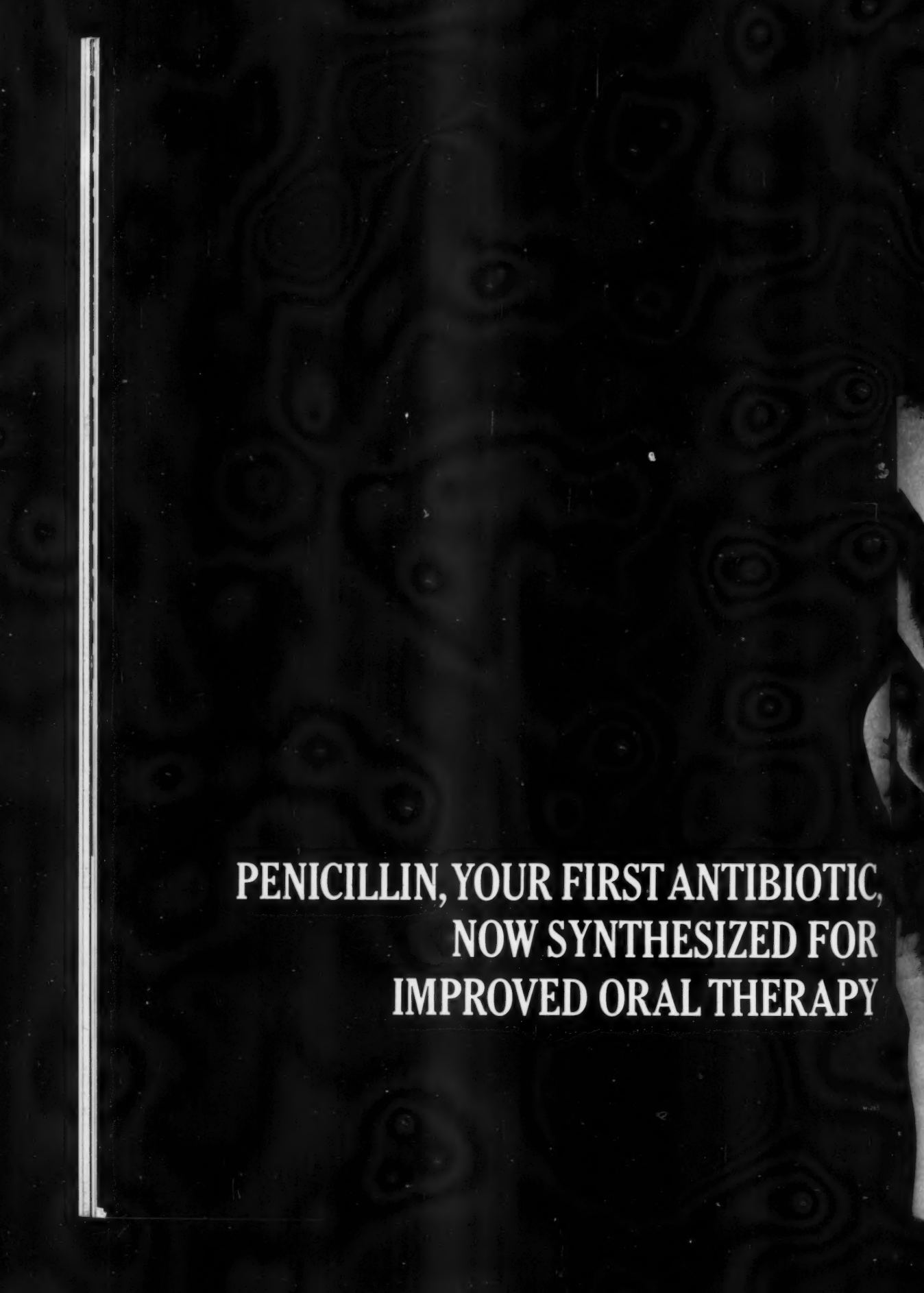
CONTRAINDICATIONS: Not to be used in cases of acute alcoholism or barbiturate poisoning.

SUPPLIED: "TIMOVAN" No. 739—25 mg. tablets. No. 740—50 mg. tablets. Bottles of 100 and 1,000.

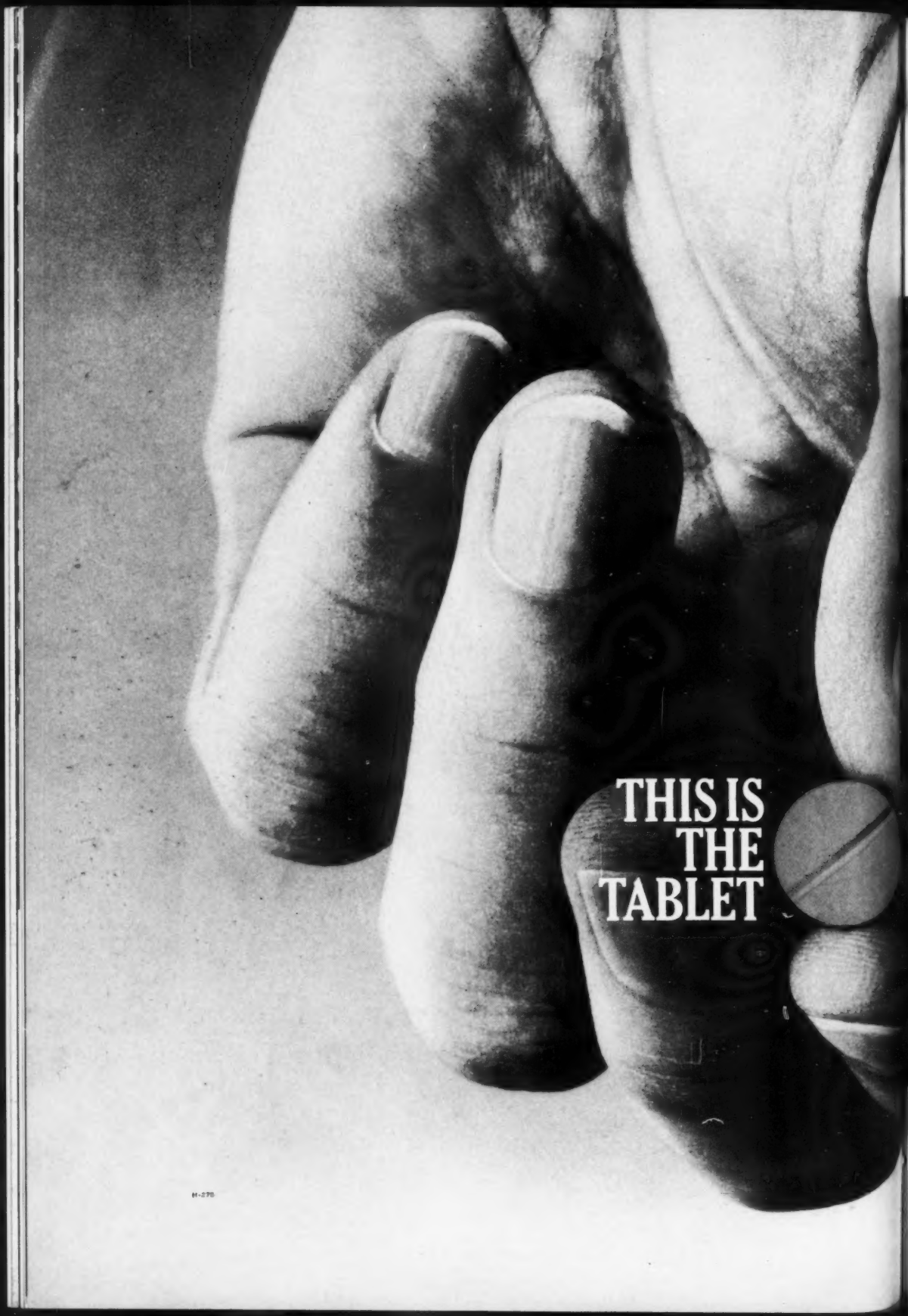
REFERENCES: 1. Medical Records of Chemiewerk Homburg A/G. 2. Linke, H.: München. med. Wchnschr. **100**:969 (June 20) 1958. 3. Quandt, V. J., Von Horn, L., and Schliep, H.: Psychiat. et Neurol. **135**:197 (Mar.) 1958. 4. Medical Records of Ayerst Laboratories.

Ayerst®

AYERST LABORATORIES
New York 16, N. Y. • Montreal, Canada


PENICILLIN, YOUR FIRST ANTIBIOTIC,
NOW SYNTHESIZED FOR
IMPROVED ORAL THERAPY

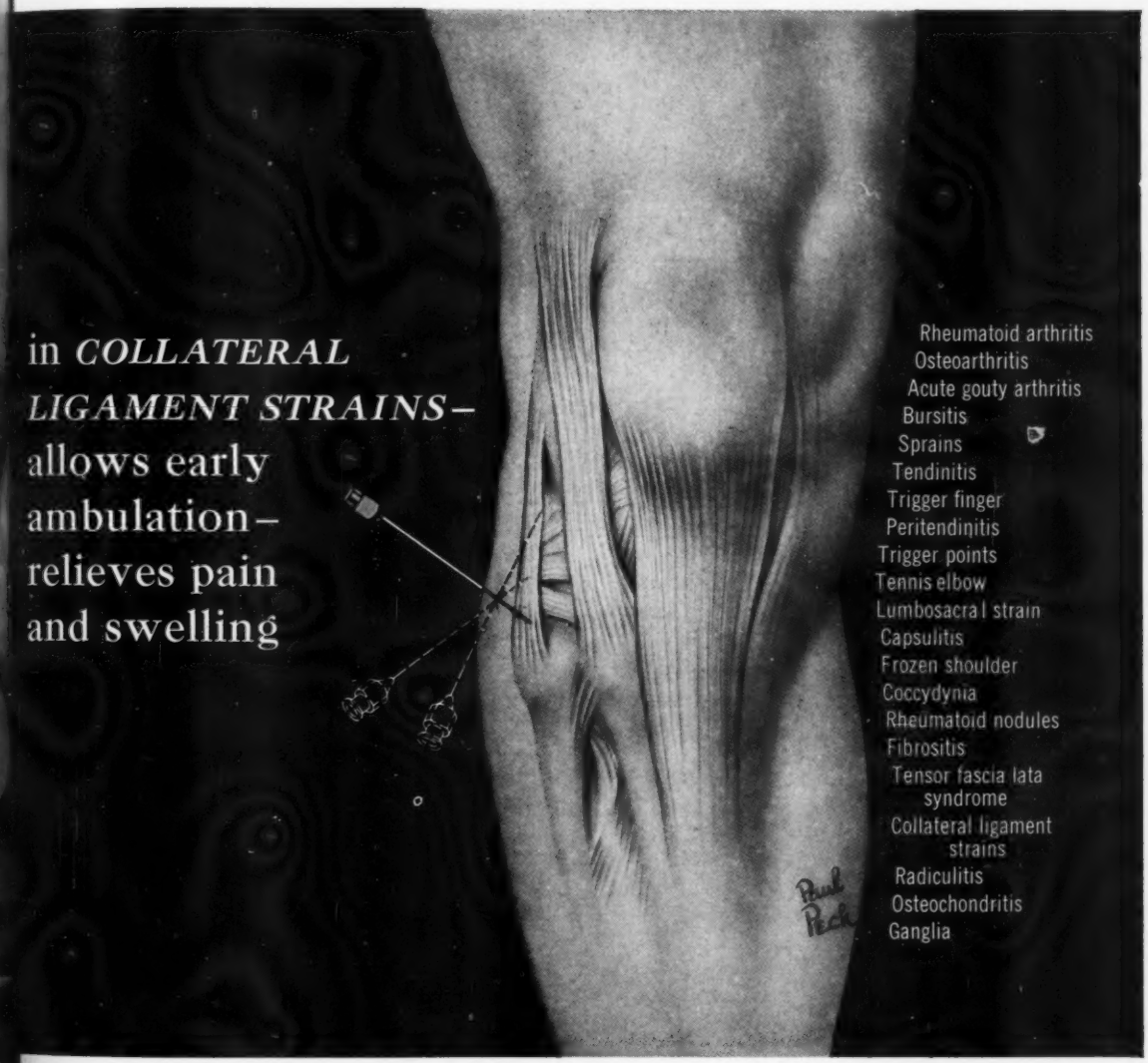
TIC,
OR
PY
THE NEW, SYNTHESIZED PENICILLIN
ALPEN
from Schering


THIS IS
THE
TABLET

HYDELTRA®-T.B.A.

(Prednisolone *tertiary*-butylacetate, Merck)

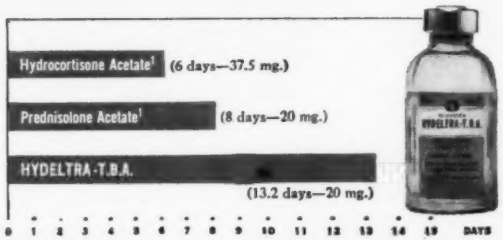
for relief that lasts – longer



in *COLLATERAL LIGAMENT STRAINS* – allows early ambulation – relieves pain and swelling

- Rheumatoid arthritis
- Osteoarthritis
- Acute gouty arthritis
- Bursitis
- Sprains
- Tendinitis
- Trigger finger
- Peritendinitis
- Trigger points
- Tennis elbow
- Lumbosacral strain
- Capsulitis
- Frozen shoulder
- Coccydynia
- Rheumatoid nodules
- Fibrositis
- Tensor fascia lata syndrome
- Collateral ligament strains
- Radiculitis
- Osteochondritis
- Ganglia

Duration of relief exceeds that provided by any other steroid ester


Hydrocortisone Acetate[1] (6 days—37.5 mg.)
Prednisolone Acetate[1] (8 days—20 mg.)
HYDELTRA-T.B.A.
(13.2 days—20 mg.)
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 DAYS

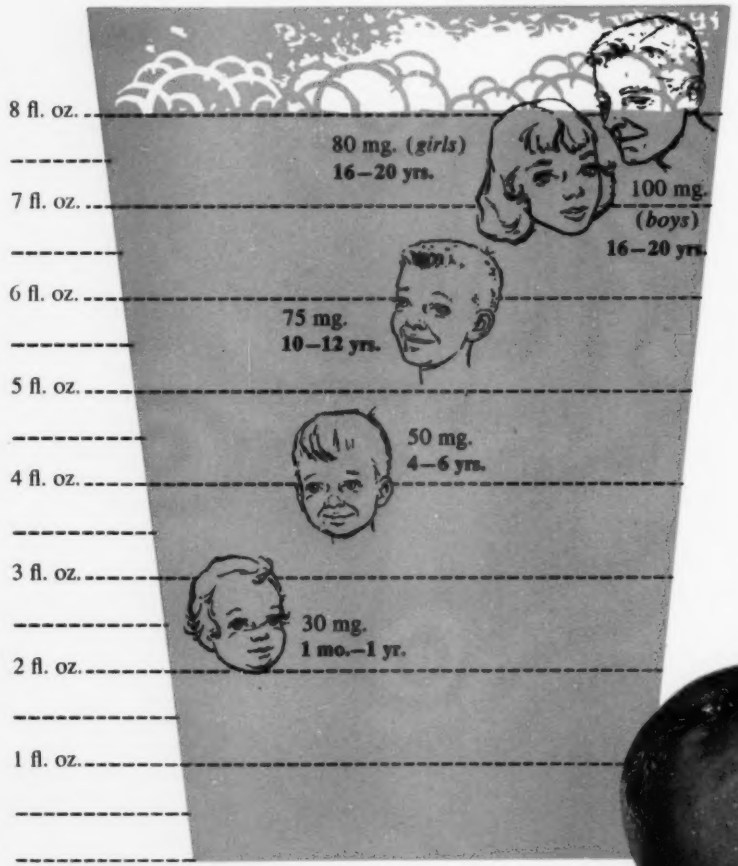
DOSAGE: the usual intra-articular, intra-bursal or soft tissue dose ranges from 20 to 30 mg. depending on location and extent of pathology.

SUPPLIED: Suspension 'HYDELTRA'-T.B.A. 20 mg./cc. of prednisolone *tertiary*-butylacetate, in 5-cc. vials.

MSD

MERCK SHARP & DOHME
DIVISION OF MERCK & CO., INC.
PHILADELPHIA 1, PA.

for developmental years
orange juice
capably supplies
recommended daily
intakes of vitamin C*



*Nat. Res. Counc., Pub. 302, 1953.

FLORIDA *Citrus*
COMMISSION • LAKELAND, FLORIDA
ORANGES • GRAPEFRUIT • TANGERINES

a significant new compound
from Mead Johnson Research

tacaryl

METHDILAZINE HYDROCHLORIDE, MEAD JOHNSON

inherently sustained action
at the cellular level
to meet the allergic attack...
with b. i. d. dosage

for prompt, prolonged relief
of allergic symptoms through
inherently sustained action at the cellular level
...with b.i.d. dosage

tacaryl™

METHDILAZINE HYDROCHLORIDE, MEAD JOHNSON

inherently sustained action
Tacaryl possesses inherent long-acting properties. After rapid disappearance from the blood stream, Tacaryl is bound to the tissues. This protective affinity for tissue provides a notably sustained effect which does not depend upon the use of artificial, long-acting construction. The sustained action is inherent to the molecule and lasts for periods up to 12 hours.

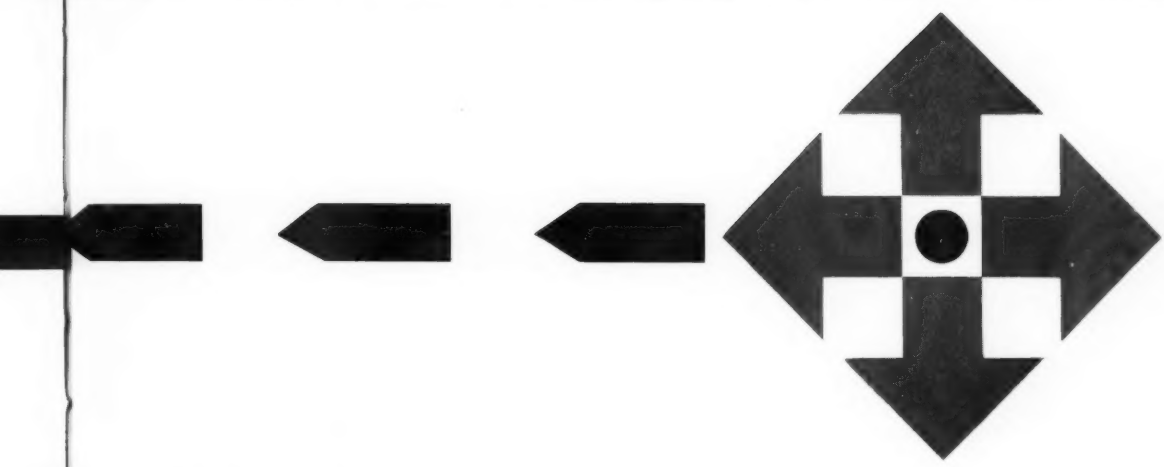
rapid absorption–rapid relief
Tacaryl is absorbed quickly to provide fast relief of symptoms. This action is due to the rapid transport of Tacaryl from the blood stream to the tissues where it exerts its action.

low toxicity–minimal side effects
In studies to date,[1] side effects were minimal; only in a small percentage of cases was mild drowsiness observed. Tolerance was not reported even after long usage. No cumulative effect has been observed.

inhibits capillary permeability and edema
Tacaryl, in laboratory animal studies, has been shown to prevent the experimental induction of pulmonary edema and cardiovascular collapse. It is also active in inhibiting the increased capillary permeability and edema produced by agents such as yeast, dextran, egg white, and serotonin.

clinically proved in a wide range of allergic and pruritic conditions
Tacaryl has provided effective symptomatic relief in a wide variety of allergic conditions among 459 patients.[1] Included were patients with nasal allergy, angioneu-

Mead Johnson
Symbol of service in medicine



rotic edema, allergic bronchial asthma and urticaria. Tacaryl has been exceptionally valuable in alleviating many types of allergic and nonallergic pruritus including that accompanying chickenpox. In some cases, the relief of itching bordered on the dramatic.[2] In a double-blind clinical evaluation[3] of various antihistaminic agents in hay fever, only Tacaryl provided benefits in all patients with moderate to severe symptoms.

effective antiallergic action in:
nasal allergies, including hay fever and allergic rhinitis • angioneurotic edema • allergic bronchitis and allergic bronchial asthma • allergic conjunctivitis • neurodermatitis • contact dermatitis • pruritus (allergic and nonallergic) • pruritus of chickenpox • urticaria • pruritus ani and vulvae

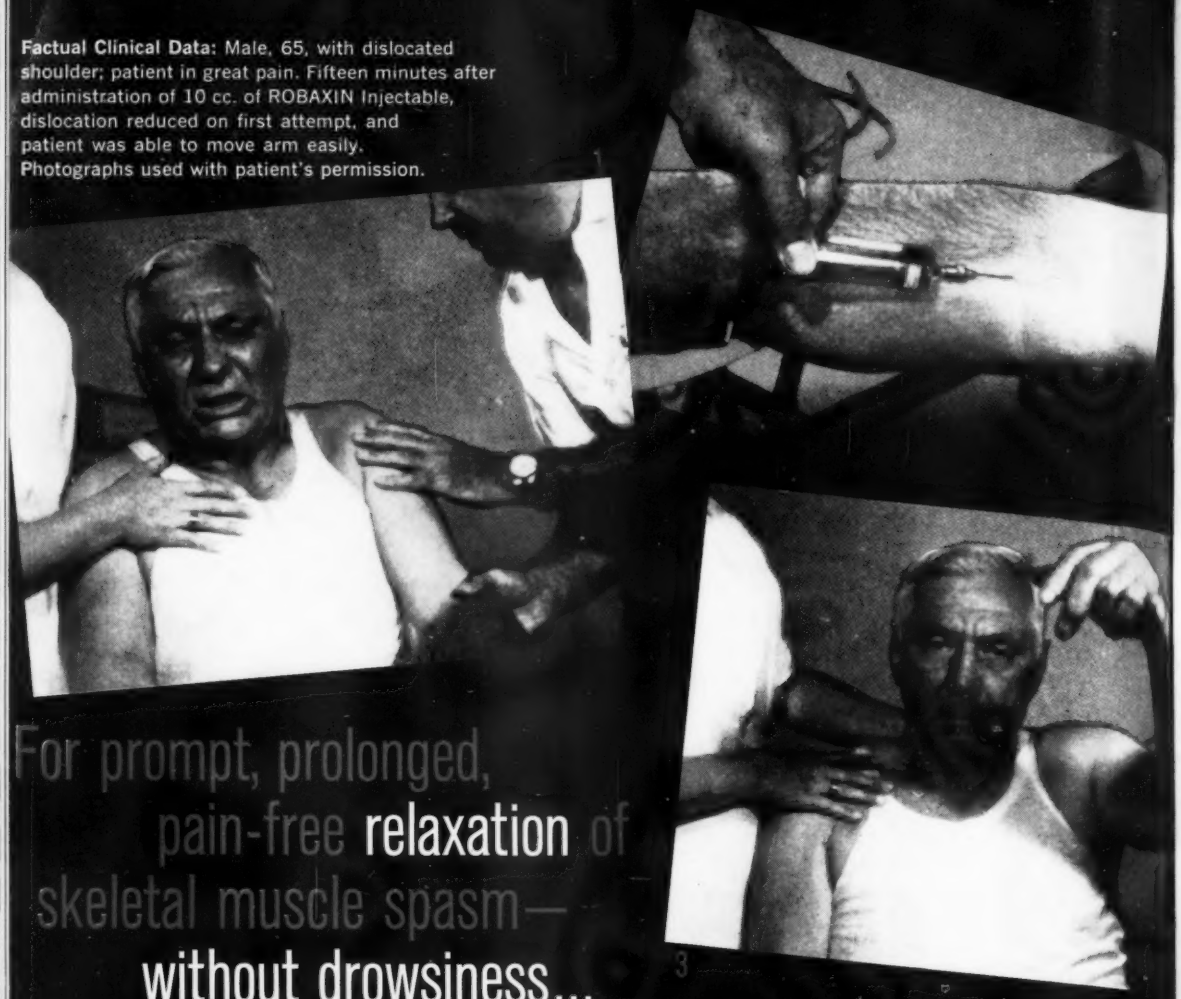
dosage
adults: Tablets—One tablet (8 mg.) twice daily.
Syrup—Two 5 cc. teaspoonfuls (8 mg.) twice daily.
children: Tablets—One-half tablet (4 mg.) twice daily.
Syrup—One 5 cc. teaspoonful (4 mg.) twice daily.
In some patients it may be desirable to adjust the dosage to meet individual requirements.

supplied
Scored tablets, 8 mg., bottles of 100. Syrup, 4 mg. per 5 cc. teaspoonful. 16 oz. bottles.

references
(1) Clinical Research Division, Mead Johnson & Company. (2) Howell, C. M., Jr.: Evaluation of Methdilazine as an Antipruritic Agent, North Carolina M. J. *21* (May) 1960 (in press). (3) Wahner, H. W., and Peters, C. A.: An Evaluation of Some Newer Antihistaminic Drugs Against Pollinosis, Proc. Staff Meet. Mayo Clin. *35*:161-169 (March 30) 1960.

21100

Factual Clinical Data: Male, 65, with dislocated shoulder; patient in great pain. Fifteen minutes after administration of 10 cc. of ROBAXIN Injectable, dislocation reduced on first attempt, and patient was able to move arm easily. Photographs used with patient's permission.



For prompt, prolonged, pain-free relaxation of skeletal muscle spasm— without drowsiness...

Robaxin®

Robins

Methocarbamol 'Robins' U.S. Pat. No. 2770649

ROBAXIN Injectable: for relaxation of painful spasm within minutes.

ROBAXIN Tablets: for initial relief, or to maintain relaxation originally induced by ROBAXIN Injectable. Virtually free from adverse side effects, including drowsiness.

Ten published studies show ROBAXIN Injectable and ROBAXIN Tablets beneficial in 91% of cases.[1-10] Literature available to physicians on request.

SUPPLY: ROBAXIN Tablets, 0.5 Gm. (white, scored) in bottles of 50 and 500.

ROBAXIN Injectable, each ampul containing 1.0 Gm. of methocarbamol in 10 cc. of sterile solution.

A. H. ROBINS CO., INC., Richmond 20, Virginia

Making today's medicines with integrity . . . seeking tomorrow's with persistence

REFERENCES: 1. Carpenter, E. S.: Southern M. J. 51:627, 1958. 2. Forsyth, H. F.: J.A.M.A. 167:63, 1958. 3. Grisolia, A., and Thomsen, J. E. M.: Clin. Orthopaedics 13:299, 1959. 4. Huggins, A. P.: Clin. Med. 6:221, 1959. 5. Lewis, W. B.: California Med. 90:26, 1959. 6. O'Doherty, D. S., and Shields, C. D.: J.A.M.A. 167:160, 1958. 7. Park, H. T.: J.A.M.A. 167:168, 1958. 8. Plumb, C. S.: Journal-Lancet 78:531, 1958. 9. Poppen, J. L., and Flanagan, M. I.: J.A.M.A. 171:298, 1959. 10. Schaupet, H. J.: Orthopedics 1:274, 1959.

Your surgical convalescent feels better because he is better with

Durabolin®

(Nandrolone phenpropionate injection, ORGANON)

for safe potent anabolic stimulation

1 cc. once each week

+ to maintain positive nitrogen balance
+ to promote rapid wound healing
+ to restore appetite, strength, vitality
+ to shorten convalescence, save nursing time
+ to reduce the cost of recovery

Supplied: 1-cc. ampuls (box of three) and 5-cc. vials, 25 mg. nandrolone phenpropionate/cc.
Adults: 1 cc. i.m. each week, or 2 cc. every other week.

Organon

ORGANON INC., W. Orange, N. J.

COUMADIN BIBLIOGRAPHY

Published studies on anticoagulant therapy with COUMADIN

1. Friedman, B.: The use of anticoagulants in the treatment of coronary and cerebral vascular disease, J. Tennessee M. A. 52:171, May, 1959. 2. Shapiro, S.: Long term therapy of coronary arteriosclerosis, Angiology 10:126, Apr., 1959. 3. Vastola, E. F., and Frugh, A.: Anticoagulants for occlusive cerebrovascular lesions, Neurology 9:143, Mar., 1959. 4. Toohey, M.: Clinical experience with warfarin sodium, Brit. M. J. 2:892, Oct. 11, 1958. 5. Porter, R. R., Richardson, D., and Mauck, H. P., Jr.: Clinical experiences with the anticoagulant warfarin sodium ("Coumadin Sodium"), Virginia M. Month. 85:465, Sept., 1958. 6. Trumble, E. A.: Clinical experience with intramuscular warfarin sodium (Coumadin Sodium), Surg. Gynec. & Obst. 107:303, Sept., 1958. 7. Goodman, D. H.: Early clue to visceral carcinoma—hemorrhage after intravenously given warfarin, J.A.M.A. 166:1037, Mar. 1, 1958. 8. Shapiro, C. M.; Lisker, R.; Lichtman, A. M., and Josephson, A. M.: Comparative clinical study of Coumadin Sodium and Dicumarol in patients with thromboembolic diseases, Am. Heart J. 55:66, Jan., 1958. 9. Yarrow, M. W.; Baer, S.; Kravitz, C., and Markson, V.: A preliminary report on sodium warfarin (Coumadin), J. Albert Einstein M. Center 5:205, June, 1957. 10. Baer, S.; Yarrow, M. W.; Kravitz, C., and Markson, V.: Clinical experiences with warfarin (Coumadin) sodium as an anticoagulant, J.A.M.A. 167:704, June 7, 1958. 11. Fremont, R. E., and Jagendorf, B.: Clinical observations on use of warfarin (Coumadin) sodium, a new anticoagulant, J.A.M.A. 165:1381, Nov. 16, 1957. 12. Shapiro, S., and Ciferri, F. E.: Intramuscular administration of the anticoagulant warfarin (Coumadin) sodium, J.A.M.A. 165:1377, Nov. 16, 1957. 13. Nicholson, J. H.: Clinical experiences with anticoagulants: A comparison of Coumadin (warfarin) Sodium and Dicumarol (bishydroxycoumarin), Angiology 8:456, Oct., 1957. 14. Kerrin, H. F.; Guidot, J., and Wilhelm, S. K.: Clinical experiences with the anticoagulant Coumadin (warfarin) Sodium, Angiology 8:302, June, 1957. 15. Goodman, D. H.: Experience with a new anticoagulant Coumadin® (warfarin) Sodium, Arizona Med. 13:389, Oct., 1956. 16. Nicholson, J. H., and Leavitt, T., Jr.: Coumadin (warfarin) Sodium: A new anticoagulant, New England J. Med. 255:491, Sept. 13, 1956. 17. Clatanoff, D. V., and Meyer, O. O.: Further observations on use of warfarin sodium in anticoagulant therapy, A.M.A. Arch. Int. Med. 97:753, June, 1956. 18. Freeman, D. J., and Meyer, O. O.: Rectal administration of warfarin (Coumadin) sodium, Sodium [3 (2-acetonyl-benzyl)-4 hydroxycoumarin], Proc. Soc. Exper. Biol. & Med. 92:52, May, 1956. 19. Pollock, B. E.: Clinical experience with Coumadin Sodium, a new anticoagulant drug, Angiology 6:506, Dec., 1955. 20. Pollock, B. E.: Clinical experience with warfarin (Coumadin) sodium, a new anticoagulant, J.A.M.A. 159:1094, Nov. 12, 1955. 21. Shapiro, S.: The hypoprothrombinemia-inducing activity of warfarin sodium (Coumadin® Sodium), J. Kansas M. Soc. 55:687, Dec. 1954. 22. Clatanoff, D. V.; Triggs, P. O., and Meyer, O. O.: Clinical experience with coumarin anticoagulants warfarin and warfarin sodium, A.M.A. Arch. Int. Med. 94:213, Aug. 1954. 23. Shapiro, S.: Warfarin sodium derivative: (Coumadin® Sodium): An intravenous hypoprothrombinemia-inducing agent, Angiology 4:380, Aug., 1953.

Other published literature referring to Endo's COUMADIN

24. Escudero, J.; McDevitt, E., and Wright, I. S.: Dicumarol, Coumadin, Marcumar and Tromexan: Comparative study of their action on the clot as registered by the thrombelastogram, Circulation 20:405, Sept., 1959. 25. Hillier, W. F., Jr.: Little strokes, West Virginia M. J. 55:259, Aug., 1959. 26. Wright, I. S.: Strokes; the present status of diagnosis and treatment. Postgrad. Med. 25:549, May, 1959. 27. Little, J. R.: Purpura fulminans treated successfully with anticoagulation, J.A.M.A. 169:104, Jan. 3, 1959. 28. Link, K. P.: The discovery of Dicumarol and its sequels, Circulation 19:97, Jan., 1959. 29. Kleiner, I. S., and Orten, J. M.: Human Biochemistry, ed. 3, Mosby, St. Louis, 1958, pp. 211-212. 30. Meyer, O. O.: Use of anticoagulants in the treatment of coronary artery disease, Postgrad. Med. 24:110, Aug., 1958. 31. Toohey, M.: Long-term anticoagulant therapy for coronary thrombosis, Brit. M. J. 2:473, Aug. 23, 1958. 32. McDevitt, E.; Wright, I. S., and Foley, W. T.: Present status of anticoagulant treatment of cerebral vascular lesions, M. Clin. North America, May, 1958, p. 587. 33. Barker, N. W.: Fundamentals of anticoagulant therapy, Minnesota Med. 41:562, Aug., 1958. 34. Grant, W. G., and MacMillan, R. L.: Experience
coagulant therapy, Canad. M. A. J. 78:317, Mar., 1958.
Treatment of peripheral arterial disease, Dis. Chest 33:
Bratman, I.: Anticoagulants in [illegible], Am.
1958. 37. Toohey, M.: Anticoagulants in myocardial infar
Feb. 1, 1958. 38. Editorial: Warfarin, Virginia M. Mon
39. Friedberg, C. K.: Recent advances in coronary heart
agement, New York J. Med. 57:3643, Nov. 15, 1957.
sodium as a long-term anticoagulant, M. Science 202,
J. H., and Oglesby, P.: Long-term anticoagulant therc
105:61, July, 1957. 42, Ware, A. G., and Stragnell,
Elimination of some commonly occurring pitfalls. Ann
1957. 43. Briner, D. H.: A study of 235 cases of myo
Osteopath. A. 56:349, Feb., 1957. 44. Cosgriff, S. W.
coronary artery disease, Am. J. Chron. Dis. 4:402,
S. A., and Aird, R. B.: M. Clin. North America, Sept.,
B. E.: The early management of myocardial infarction,
1956. 47. Shapiro, S.: Anticoagulant therapy, Surg.
1956, p. 469. 48. Wright, I. S.: Present status of an
treatment of myocardial infarction; the use and mis
evaluation of new anticoagulants, their indications a
43:942, Nov., 1955. 49. Shapiro, S. (editorial): The a
prothrombinemia-inducing drugs, Angiology 6:498, Oc
Principles of anticoagulant therapy and their applicat
ica, Jan., 1955, p. 227. 51. Shapiro, S., and Spitzer,
(ascorbic acid plus "P" factors) in drug-induced hypo
ology 5:64, Apr. 1954.

Coumadin is the original and only warfarin sodium responsible for establishing this drug as "the best anticoagulant available today"[30]

(over 50 published papers since 1953)

COUMADIN®

FOR ORAL, INTRAVENOUS OR INTRAMUSCULAR USE

SODIUM

IN MYOCARDIAL INFARCTION AND OTHER THROMBOEMBOLIC DISORDERS

SUPPLIED: ***Oral***—scored tablets, 2 mg., 5 mg., 7½ mg., 10 mg., 25 mg. ***Parenteral***—single injection units, consisting of one vial, 75 mg., and one 3-cc. ampul Water for Injection.

COUMADIN (warfarin) Sodium is manufactured under license from the Wisconsin Alumni Research Foundation... *clinically established by Endo.*

Complete Information and Reprints on Request

ENDO LABORATORIES
Richmond Hill 18, New York

Over 60,000,000 doses of Coumadin administered to date

as it calms anxiety!

Smooth, balanced action lifts depression as it calms anxiety... rapidly and safely

Balances the mood – no "seesaw" effect of amphetamine-barbiturates and energizers. While amphetamines and energizers may stimulate the patient – *they often aggravate anxiety and tension.*

And although amphetamine-barbiturate combinations may counteract excessive stimulation – *they often deepen depression.*

In contrast to such "seesaw" effects, Deprol's smooth, *balanced* action lifts depression as it calms anxiety – both at the same time.

Acts swiftly – the patient often feels better, sleeps better, within a few days. Unlike the delayed action of most other antidepressant drugs, which may take two to six weeks to bring results, Deprol relieves the patient quickly –often within a few days. Thus, the expense to the patient of long-term drug therapy can be avoided.

Acts safely – no danger of liver damage. Deprol does not produce liver damage, hypotension, psychotic reactions or changes in sexual function–frequently reported with other antidepressant drugs.

Bibliography *(13 clinical studies, 858 patients)*: **1.** Alexander, L. (35 patients): Chemotherapy of depression – Use of meprobamate combined with benactyzine (2-diethylaminoethyl benzilate) hydrochloride. J.A.M.A. 166:1019, March 1, 1958. **2.** Bateman, J. C. and Carlton, H. N. (50 patients): Meprobamate and benactyzine hydrochloride (Deprol) as adjunctive therapy for patients with advanced cancer. Antibiotic Med. & Clin. Therapy 6:648, Nov. 1959. **3.** Beerman, H. M. (44 patients): The treatment of depression with meprobamate and benactyzine hydrochloride. Western Med. 1:10, March 1960. **4.** Bell, J. L., Tauber, H., Santy, A. and Pulito, F. (77 patients): Treatment of depressive states in office practice. Dis. Nerv. System 20:263, June 1959. **5.** Breitner, C. (31 patients): On mental depressions. Dis. Nerv. System 20:142, (Section Two), May 1959. **6.** Gordon, P. E. (50 patients): Deprol in the treatment of depression. Dis. Nerv. System 21:215, April 1960. **7.** Landman, M. E. (50 patients): Clinical trial of a new antidepressive agent. J. M. Soc. New Jersey. In press, 1960. **8.** McClure, C. W., Papas, P. N., Speare, G. S., Palmer, E., Slattery, J. J., Konefal, S. H., Henken, B. S., Wood, C. A. and Ceresia, G. B. (128 patients): Treatment of depression – New technics and therapy. Am. Pract. & Digest Treat. 10:1525, Sept. 1959. **9.** Pennington, V. M. (135 patients): Meprobamate-benactyzine (Deprol) in the treatment of chronic brain syndrome, schizophrenia and senility. J. Am. Geriatrics Soc. 7:656, Aug. 1959. **10.** Rickels, K. and Ewing, J. H. (35 patients): Deprol in depressive conditions. Dis. Nerv. System 20:364, (Section One), Aug. 1959. **11.** Ruchwarger, A. (87 patients): Use of Deprol (meprobamate combined with benactyzine hydrochloride) in the office treatment of depression. M. Ann. District of Columbia 28:438, Aug. 1959. **12.** Settel, E. (52 patients): Treatment of depression in the elderly with a meprobamate-benactyzine hydrochloride combination. Antibiotic Med. & Clin. Therapy 7:28, Jan. 1960. **13.** Splitter, S. R. (84 patients): Treatment of the anxious patient in general practice. J. Clin. & Exper. Psychopath. In press, April-June 1960.

▲Deprol▲®

Dosage: Usual starting dose is 1 tablet q.i.d. When necessary, this dose may be gradually increased up to 3 tablets q.i.d.

Composition: 1 mg. 2-diethylaminoethyl benzilate hydrochloride (benactyzine HCl) and 400 mg. meprobamate. **Supplied:** Bottles of 50 light-pink, scored tablets. Write for literature and samples.

WALLACE LABORATORIES / *New Brunswick, N. J.*

CG-2127

why not re-evaluate PORK

in the light of today's scientific findings–

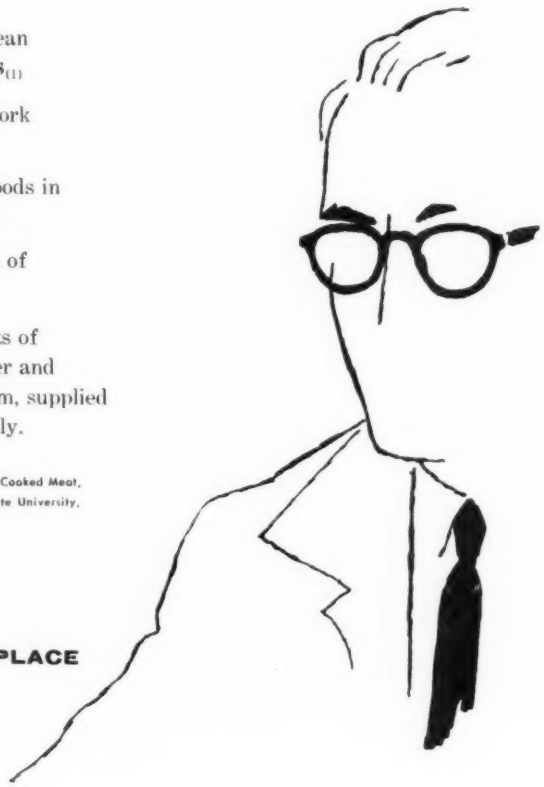
the average serving of 100 gm. of lean pork provides a **modest** 250 **calories**(1)

—compare the **fat-content** of lean pork with that of other lean meats.

—pork outranks other high-protein foods in its **contribution of thiamine** (B_1)

—pork provides an important amount of **other B vitamins**

—pork contributes significant amounts of the **essential minerals,** iron, copper and phosphorus, magnesium and potassium, supplied in a form that the body can use readily.



1. Leverton, R. M., and Odell, G. V.: The Nutritive Value of Cooked Meat, Oklahoma Agricultural Experiment Station, Oklahoma State University, Miscellaneous Publication MP-49, 1958.

PUT PORK IN ITS PROPER PLACE

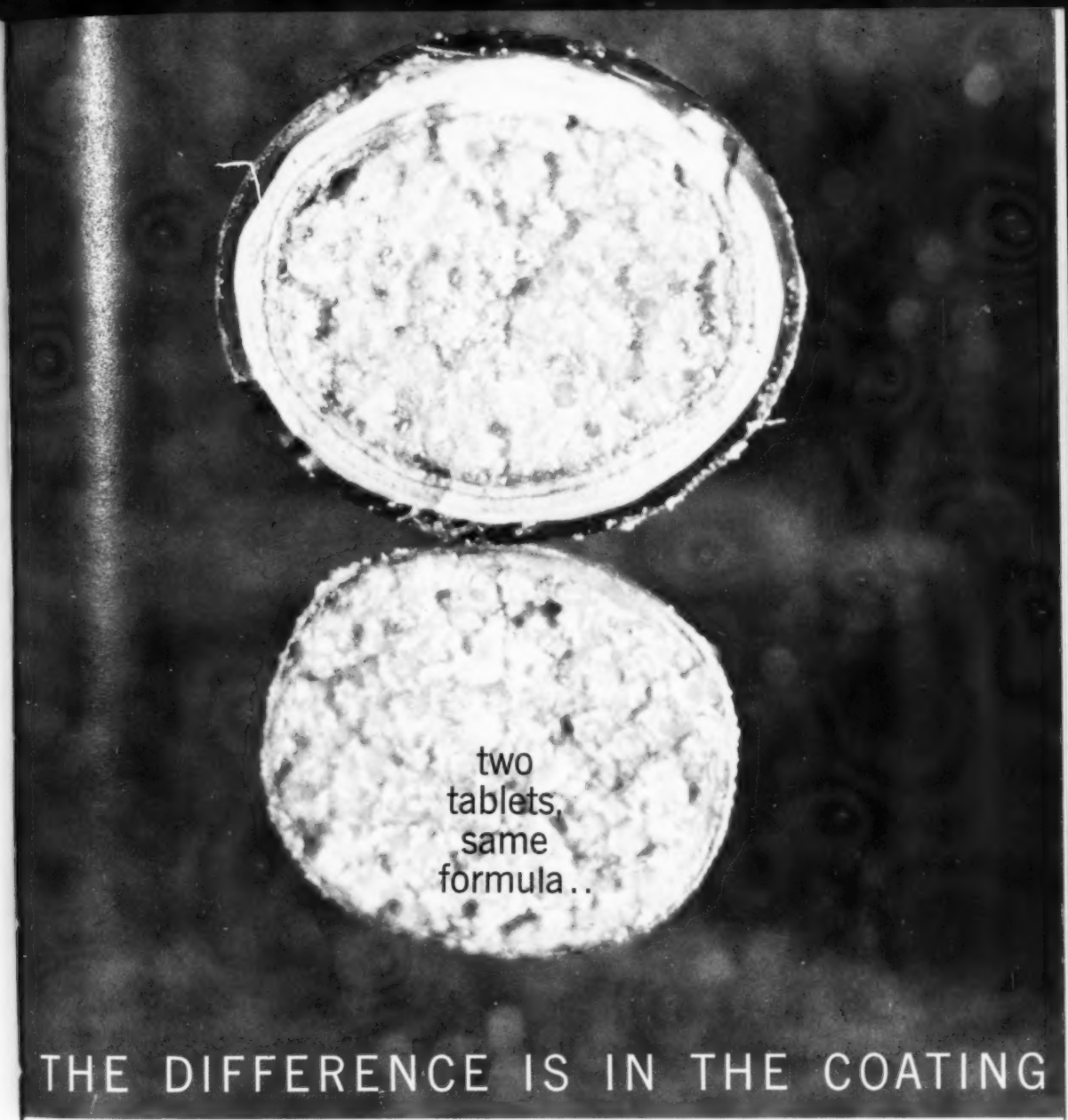
. . . in the daily diet

. . . use to tempt jaded appetites

The nutritional statements made in this advertisement have been reviewed by the Council on Foods and Nutrition of the American Medical Association and found consistent with current authoritative medical opinion.

AMERICAN MEAT *INSTITUTE*

MAIN OFFICE, CHICAGO • MEMBERS THROUGHOUT THE NATION



THE DIFFERENCE IS IN THE COATING

FILMTAB—FILM-SEALED TABLETS, ABBOTT 004032A
©1960—ABBOTT LABORATORIES, NORTH CHICAGO, ILLINOIS

Above: An enlarged (16X) sectional view of the original Dayalets-M tablet with standard sugar coating. Below: Today's Filmtab Dayalets-M has the same formula, but 30% less bulk.

With a picture like we see above, you can get a pretty good idea of what happens when we put a Filmtab coating on one of our Abbott vitamins. The change in size is noticeable, to say the least.

There's nothing mysterious about it. With sugar coatings, you need several coats and sub-coats to build up a durable, evenly-rounded tablet. With Filmtab, all you need is the Filmtab itself.

Is it durable? Well, the chances are good that Filmtab coating will outlast most sugar coatings. For one thing, the Filmtab process is non-aqueous. Hydrolysis simply cannot occur. Also, you do away with tablet "brittleness." These Filmtab vitamins won't chip, crack or stick. And the seal is perfect: No vitamin taste or odor, ever.

Filmtab—on "Vitamins by Abbott."

ABBOTT

Vitamins by Abbott in a rainbow of brilliant colors

FILMTAB DAYALETS® TABLE BOTTLE (100'S); BOTTLES OF 50 & 250
FILMTAB DAYALETS-M®
APOTHECARY BOTTLES 100 & 250

Extra-potent maintenance formulas, ideal for the nutritionally "run-down"

each Filmtab **DAYALETS** represents:

Vitamin A	3 mg. (10,000 units)
Vitamin D	25 mcg. (1000 units)
Thiamine Mononitrate	5 mg.
Riboflavin	5 mg.
Nicotinamide	25 mg.
Pyridoxine Hydrochloride	2 mg.
Vitamin B_{12} (as cobalamin concentrate)	2 mcg.
Folic Acid	0.25 mg.
Calcium Pantothenate	5 mg.
Ascorbic Acid	100 mg.

Dosage: Just one Filmtab daily for prophylaxis; two or more daily for therapeutic effect.

each **DAYALETS-M** represents all of Dayalets' vitamins, plus the following:

Iron (as sulfate)	10 mg.
Copper (as sulfate)	1 mg.
Iodine (as calcium iodate)	0.15 mg.
Cobalt (as sulfate)	0.1 mg.
Manganese (as sulfate)	1 mg.
Magnesium (as oxide)	5 mg.
Potassium (as sulfate)	5 mg.
Zinc (as sulfate)	1.5 mg.
Molybdenum (as sodium molybdate)	0.2 mg.

Dosage: One Filmtab daily, or as directed by physician.

0040328

FILMTAB OPILETS®
FILMTAB OPTILETS-M®
TABLE BOTTLES OF 30 & 100.
BOTTLES OF 1000.

Therapeutic formulas for more severe deficiencies—illness, infection, etc.

each **OPTILETS** Filmtab represents:

Vitamin A	7.5 (25,000 units)
Vitamin D	25 mcg. (1000 units)
Thiamine Hydrochloride	10 mg.
Riboflavin	5 mg.
Nicotinamide	100 mg.
Pyridoxine Hydrochloride	5 mg.
Folic Acid	0.3 mg.
Vitamin B_{12} (as cobalamin concentrate)	6 mcg.
Calcium Pantothenate	20 mg.
Ascorbic Acid	200 mg.

Dosage: One or two Filmtabs daily, or as directed by the physician.

each **OPTILETS-M** represents all the vitamins of Optilets, plus the following:

Iron (as sulfate)	10 mg.
Copper (as sulfate)	1 mg.
Iodine (as calcium iodate)	0.15 mg.
Cobalt (as sulfate)	0.1 mg.
Manganese (as sulfate)	1 mg.
Magnesium (as oxide)	5 mg.
Potassium (as sulfate)	5 mg.
Zinc (as sulfate)	1.5 mg.
Molybdenum (as sodium molybdate)	0.2 mg.

Dosage: One or two Filmtabs daily, as directed by physician.

Five quality formulas to fit every nutritional need
Filmtab coating to cut size and assure potency
Table bottles (at no extra cost)

FILMTAB SUR-BEX® WITH C
TABLE BOTTLE OF 60.
BOTTLES OF 100, 500 & 1000.

Therapeutic B-complex formula with C, for convalescence, stress, post-surgery

each **SUR-BEX WITH C** Filmtab represents:

Thiamine Mononitrate	6 mg.
Riboflavin	6 mg.
Nicotinamide	30 mg.
Pyridoxine Hydrochloride	1 mg.
Vitamin B_{12} (as cobalamin concentrate)	2 mcg.
Calcium Pantothenate	10 mg.
Ascorbic Acid	150 mg.
Desiccated Liver, N.F.	300 mg.
Brewer's Yeast, Dried	150 mg.

Dosage: As a dietary supplement, 1 or 2 Filmtabs daily; in convalescence, 2 or more Filmtabs daily.

ABBOTT

N UROPATHIES

HEN PAIN IS PART OF THE PICTURE

inary tract pain, at the source or referred, is subject to the rapid algesic action of the azo dye in Azo Gantrisin. Azo Gantrisin combines matic relief of symptoms with proven effective action against infec- ns carried by either blood stream or urine.

luable also following urologic manipulation and surgery.

AZO GANTRISIN

NTRISIN®—brand of sulfisoxazole ROCHE®

Diagram correlates sources of primary urinary pain with areas of referred pain.

Dosage: Adults—2 tablets four times daily.
Children under 100 lbs—1 tablet four times daily.
Each tablet provides 0.5 Gm Gantrisin plus 50 mg phenylazodiamino-pyridine HCl—bottles of 100 and 500.

ROCHE LABORATORIES
Division of Hoffmann-La Roche Inc.
Nutley 10, N. J.

how does* Mellaril *differ from other potent tranquilizers?

Mellaril®

THIORIDAZINE HCl
specific, effective tranquilizer

provides highly effective tranquilization,
relieves anxiety, tension, nervousness,
but is virtually free of such toxic effects as

jaundice
Parkinsonism
blood dyscrasia
dermatitis

greater specificity of tranquilizing action results in fewer side effects

Virtual freedom of Mellaril from major toxic effects is due to greater specificity of tranquilizing action — divorced from such "diffuse" effects as anti-emetic action.

"The most striking aspect of thioridazine [MELLARIL] therapy is the poverty of side-effects."

"In conclusion it may be said that thioridazine is at least as effective in relieving psychiatric illness as other drugs of its class. On a milligram for milligram basis it has the same order of potency as chlorpromazine. In its low incidence of side-effects and toxicity, it is superior to all other tranquilizing drugs tested. For this reason it is well tolerated by patients, particularly those who are not hospitalized and who frequently discontinue their medication with other drugs because of dizziness, sleepiness, increased tension, or Parkinsonism."*

Supply: MELLARIL Tablets, 10 mg., 25 mg., 100 mg.

SANDOZ

*Gross-Wright, J.: Newer phenothiazine drugs in treatment of nervous disorders, J.A.M.A. 170:1283, July 11, 1959.

There's hardly a reason *not* to prescribe Doriden
for every patient who needs a good night's sleep
DORIDEN® (glutethimide CIBA)
CIBA
SUMMIT, N.J.

Why you can prescribe DORIDEN® for nearly all insomnia patients

Because it acts smoothly, because it is metabolized rapidly, because it apparently has no toxic effect on the liver or kidney, Doriden is indicated in many cases where barbiturates are unsuitable. With Doriden, for example, you can prescribe a good night's sleep for patients sensitive to barbiturates, elderly patients, patients with low vital capacity and poor respiratory reserve, and those unable to take barbiturates because of renal or hepatic disease. And Doriden patients awake refreshed—except in rare cases, there's no morning "hangover."

SUPPLIED: *Tablets,* 0.5 Gm., 0.25 Gm. and 0.125 Gm.

CIBA
SUMMIT • NEW JERSEY

DORIDEN® (glutethimide CIBA)

3/2761HB

containing Oxethazaine
a gastric mucosal
anesthetic

OXAINE*

Oxethazaine in Alumina Gel, Wyeth

for gastritis

an original development,
backed by 5 years' research
and clinical trial

OXAINE contains a gastric mucosal anesthetic for the relief of pain of gastritis.

OXAINE is indicated in the many patients who do not respond to diet, antacids and anticholinergics.

As reported in J.A.M.A., OXAINE brought complete relief to 96% of 92 gastritis patients suffering substernal pain and upper abdominal distress.
Deutsch, E., and Christian, H. J.: J.A.M.A. 169:*2012 (April 25) 1959.*

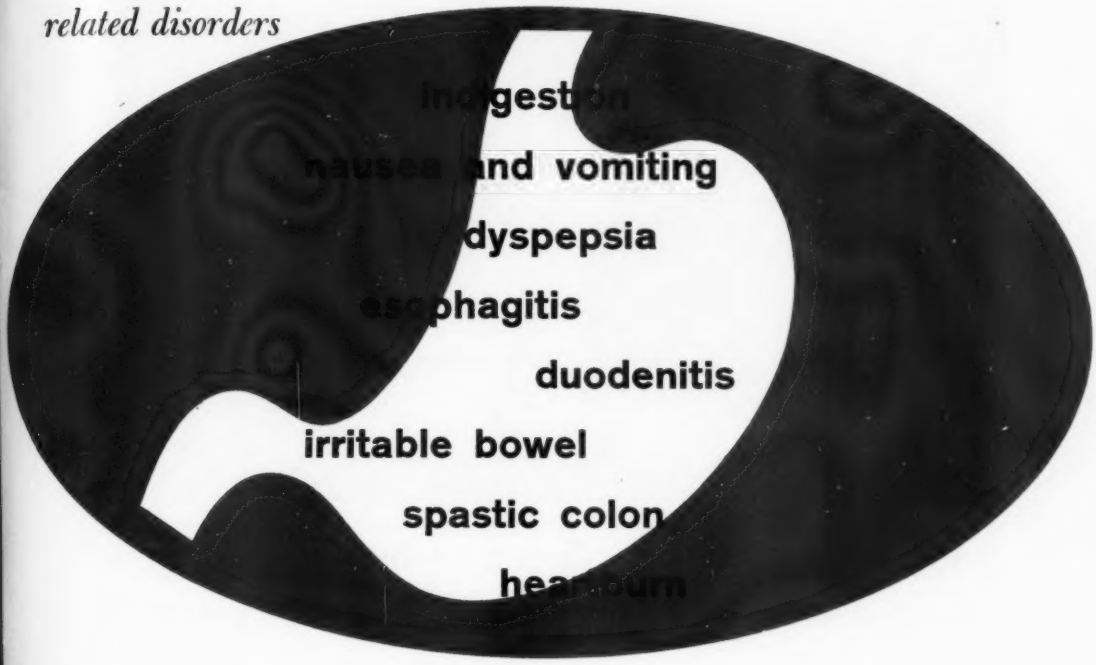
OXAINE provides sustained anesthesia over many hours, unaffected by ebb and flow of gastric contents.

Oxethazaine, the mucosal anesthetic in OXAINE, is 4000 times more potent topically than procaine. Safe, not a "caine." Only two known cases of sensitivity (glossitis) occurred in extensive clinical trials.

Easily administered, simple dosage—just 2 teaspoonfuls 15 minutes before meals and at bedtime.

Bland, noncloying over long-term administration.

related disorders



How OXAINE *Relieves Pain, Hastens Recovery*

Gastric mucosa can heal more quickly, because local anesthetics inhibit acid and pepsin secretion, by preventing release of *gastrin* from the antrum of the stomach.

Patients tolerate a more varied diet and a larger amount of food—and, because of OXAINE, enjoy their food without fear of pain following meals.

They feel free of bloating and the disturbing sensation of fullness when only a little food has been ingested—because the anesthesia of OXAINE desensitizes irritated nerve receptors.

Those with irritable bowel syndrome are spared the embarrassing urge to defecate during meals —because OXAINE diminishes the exacerbated gastrocolic reflex.

Supplied: *In bottles of 12 fluidounces.*

Wyeth Laboratories Philadelphia 1, Pa.

100 ANNIVERSARY Wyeth

A Century of Service to Medicine

Helps you take the misery out of menopause

as hormones alone often don't do

Fast-acting Milprem directly relieves both emotional dread and estrogen deficiency

Dosage: One Milprem tablet t.i.d. in 21-day courses with one-week rest periods; during the rest periods, Miltown alone can sustain the patient.

Composition: Miltown (meprobamate) + conjugated estrogens (equine).

Supplied: **Milprem-400**, each coated pink tablet contains 400 mg. Miltown and 0.4 mg. conjugated estrogens (equine). **Milprem-200**, each coated old-rose tablet contains 200 mg. Miltown and 0.4 mg. conjugated estrogens (equine). Both potencies in bottles of 60.

Literature and samples on request.

Many physicians find that estrogen therapy is not enough for the woman who is also filled with anxiety by her menopause. Her emotional dread may make her so miserable that it becomes a real clinical problem.

This is where Milprem helps you so much. It calms the woman's anxiety and tension; prevents moody ups and downs; relieves her insomnia and headache. At the same time, it checks hot flushes by replacing lost estrogens. The patient feels better than she did on estrogen therapy alone. And your counsel and your assurances can now help her make her adjustment much faster.

Milprem®

(Miltown® plus natural estrogens)

CMP-1306

WALLACE LABORATORIES / *New Brunswick, N. J.*

Why Clinical Judgment Often Dictates Altafur for Peroral, Systemic Therapy of Pyodermas

Gratifying Therapeutic Response

ALTAFUR was found "highly satisfactory in most of the primary and secondary bacterial dermatoses treated to date," including "pyodermas . . . caused by antibiotic resistant strains of staphylococci."[1] In a nationwide survey[2] there were **94%** satisfactory results (cured or improved) among 159 patients treated with ALTAFUR for pyodermas.

Virtually Uniform in vitro Susceptibility of Staphylococcus aureus

99.5% of isolates (214 of 215) from patients with staphylococcal infections—including many antibiotic-resistant strains—proved sensitive in vitro to ALTAFUR in tests conducted across the nation.[3] **99.7%** of staphylococcal isolates (334 of 335) at a large general hospital—including many antibiotic-resistant strains—proved sensitive in vitro to ALTAFUR.[4]

Wide, Stable Antimicrobial Spectrum

"Because of its relationship to previously developed nitrofurans, it is anticipated that [ALTAFUR] will retain its original spectrum after longstanding clinical usage."[5] Development of significant bacterial resistance to ALTAFUR has not been encountered to date.[6]

Minimal Side Effects

Side effects are easily avoided or minimized by these simple precautions: 1) *alcohol should not be ingested in any form, medicinal or beverage, during* ALTAFUR *therapy and for one week thereafter* 2) each dose should be taken with or just after meals, and with food or milk at bedtime (to reduce the likelihood of occasional nausea and emesis).

---

1. Weiner, A. L.: Paper presented at the Conference on Recent Advances in the Treatment of Chronic Dermatoses, University of Cincinnati (Ohio), Nov. 5, 1959. 2. Compiled by the Medical Department, Eaton Laboratories, from case histories received. 3. Christenson, P. J., and Tracy, C. H.: Current Therapeutic Research 2:22, 1960. 4. Glas, W. W., and Britt, E. M.: Proceedings of the Detroit Symposium on Antibacterial Therapy, Michigan and Wayne County Academies of General Practice, Detroit, Sept. 12, 1959, p. 14. 5. Leming, B. H., Jr.: Ibid., p. 22. 6. Investigators' reports to the Medical Department, Eaton Laboratories.

Tablets of 250 mg. (adult)

and 50 mg. (pediatric)

bottles of 20 and 100

Altafur®

NITROFURANS . . . a unique class of antimicrobials

EATON LABORATORIES, NORWICH, NEW YORK

in your first instructions for the newborn... as basic as the bath...VI-SOL™ VITAMIN DROPS

Baby's bath—basic to help guard against infections. Vi-Sol drops—basic to help guard against vitamin deficiencies from the very first visit. Why Vi-Sol drops? Because they are quality formulations of acknowledged potency, safety and acceptability, in line with the Mead Johnson tradition of product leadership in infant nutrition. Products of choice in premature centers—dynamic retail product movement provides added assurance of freshness, readily accepted by mother and baby alike—three authoritative formulations to meet individual nutritional needs...these are but a few of the outstanding features that have made Vi-Sol drops one of the most popular of all infant vitamin supplements. You select the formulation—3, 6 or 10 vitamins to suit individual needs:

TRI-VI-SOL® drops—3 basic vitamins;

POLY-VI-SOL® drops—6 essential vitamins;

DECA-VI-SOL® drops—10 significant vitamins.

Mead Johnson
Symbol of service in medicine
EVANSVILLE 21, INDIANA
92960

when your ambulatory patient's problem is **excessive gas...**

ILOPAN-CHOLINE

tablets • Warren-Teed

POSTCHOLECYSTECTOMY • SPLENIC FLEXURE SYNDROME
POST INTESTINAL RESECTION • POST ANTIBIOTIC FLATULENCE
GERIATRIC DIGESTIVE FAILURE • INFECTIOUS HEPATITIS

These are but a few of the many conditions in which flatulence due to intestinal atony is often a complicating and discomforting factor. » Three independent clinical evaluations of patients aged 20 to 80, proved ILOPAN-CHOLINE 90% effective in preventing and relieving retention and distention caused by intestinal atony. » Each ILOPAN-CHOLINE tablet contains 50 mg. d-pantothenyl alcohol — key substance of the coenzyme A molecule required for acetylation, and 25 mg. choline bitartrate — parent substance of acetylcholine essential for peristaltic efficiency.

Dosage — 2 tablets, t.i.d. Contraindications — none known. Supplied — bottles of 100 and 500.

THE WARREN-TEED PRODUCTS COMPANY

Dallas Chattanooga COLUMBUS, OHIO Los Angeles Portland

Unless your practice is limited to bacteriology . . . or your patients are all in the upper income brackets . . . you have doubtless received complaints about the cost of the medication you prescribe.

what your patient

gives...and gets

Some of these complaints can probably be dismissed lightly as coming from cranks, who would complain about your fee for a midnight house call to save the life of a dying child. Others, however, are made seriously by thoughtful patients and deserve an answer in kind. You know what the patient gets from his pharmacist because you have prescribed it. Do you also know that the average cost of a prescription is about $3.00? Only about one in 100 costs $10.00 or more, and 3 out of 5 of the prescriptions are under $3.00. These figures are based on retail prices. They include the manufacturer's research, development, and manufacturing costs and all distribution costs of the wholesale and the retail druggist. Only you and your patients can judge whether today's drugs at these prices represent a fair *quid pro quo,* an equitable balance between what is given and what is received.

This message is brought to you by 138 producers of prescription drugs as a service to the medical profession and in the same spirit, it is carried by this publication. For additional information, please write Pharmaceutical Manufacturers Association, 1411 K Street, N.W., Washington 5, D.C.

Kolantyl

is much more than an antacid

Clinical experience clearly indicates that alkali is not the only answer to ulcer pain.[1-5]

More than an antacid is needed. Kolantyl is more than an antacid. It blocks all *three* sources of ulcer pain. An antispasmodic (safe Bentyl) to stop pain-producing spasm. Anti-enzyme action to curb peptic erosion. Balanced antacids that neither constipate nor laxate. Plus a demulcent to promote healing.

TRADEMARKS: BENTYL®, KOLANTYL®

Shotgun therapy? Probably not, when you consider this: Which one of the ingredients of Kolantyl can an ulcer patient do without?

Dosage: 1 tablespoon, or 2 tablets, every three hours, as needed.

REFERENCES: 1. Altschule, Mark D.: Med. Science 6:560, Oct. 25, 1959. **2.** Kasich, A. M.; Boleman, A. P., Jr., and Rafsky, J. C.: Am. J. Digest. Dis. 1:361, 1956. **3.** Roth, J. L. A.; Wechsler, R. L., and Bockus, H. L.: Gastroenterology 31:493, 1956. **4.** Rafsky, J. C.: Gastroenterology 27:29, 1954. **5.** Ruffin, J. M.; Baylin, G. J.; Legerton, C. W., and Texter, E. C., Jr.: Gastroenterology 23:252, 1953.

THE WM. S. MERRELL COMPANY New York • Cincinnati • St. Thomas, Ontario

Merrell

analgesia in depth

Announcing **Equagesic®**

TABLETS

meprobamate and ethoheptazine citrate with acetylsalicylic acid, Wyeth

Relieves Pain · Relieves Anxiety · Relieves Muscle Tension

Equagesic

—the first non-narcotic preparation
to fulfill all requirements
of analgesia in depth

EQUAGESIC provides:

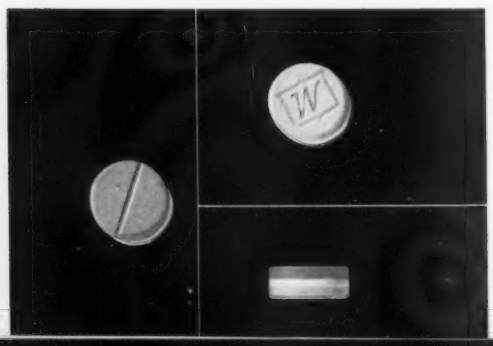
1. **Relief of pain**
2. **Relief of the anxiety which magnifies pain**
3. **Relief of the muscle tension and spasm which add pain to pain**

EQUAGESIC combines **EQUANIL**® (meprobamate) with ethoheptazine citrate and acetylsalicylic acid, the latter agents available separately as **ZACTIRIN**®.

EQUANIL is the proved, preeminent, muscle-relaxant and antianxiety agent. **ZACTIRIN** is a non-narcotic analgesic, highly effective in painful disorders commonly treated in office practice.

Prior to introduction, **EQUAGESIC** underwent extensive clinical trial. A total of 463 physicians reported on 2,816 patients. Among 40 symptom complexes treated were disorders of the bones and skeletal muscles, particularly traumatic and arthritic conditions; headache, dysmenorrhea, neuritis, and neuralgia.

"Moderate to severe" pain occurred in 90.4% of the patients studied, 3.8% of the patients experiencing "mild" pain, and the remaining 5.8% "very severe" pain. Results of this extended clinical evaluation are highlighted in the tables opposite.



Optimum initial dose of **EQUAGESIC** is 2 tablets 3 to 4 times a day. Frequently, only 1 tablet 3 to 4 times a day will suffice. Supplied: In bottles of 50 scored tablets; each containing 150 mg. of meprobamate (white layer), 75 mg. ethoheptazine citrate (yellow layer), and 250 mg. acetylsalicylic acid (pink layer).

Degree of Relief from Pain

Degree of Relief	% of Total Patients
Complete Relief	29.4
Most Pain Relieved	49.8
Most Pain Remained	11.5
No Relief	9.3
	100.0

Relief from Pain Compared to Analgesic Previously Used

(Was reported in 1,927, or 68.4% of patients.)

Relief from Pain	% of Total Patients
Superior	60.6
Equal	28.4
Inferior	11.0
	100.0

Degree of Relief from Muscle Spasm

(Was reported in 2,074, or 73.6% of patients.)

Degree of Relief	% of Total Patients
Complete Relief	32.3
Most Spasm Relieved	48.0
Most Spasm Remained	12.3
No Relief	7.4
	100.0

Relief from Spasm as Compared to Previous Muscle Relaxant

(Was reported in 998, or 35.4% of patients.)

Relief from Spasm	% of Total Patients
Superior	53.2
Equal	38.1
Inferior	8.7
	100.0

Undesirable Effects

2,590 patients, or 92.0%, reported no side effects.
226 patients, or 8.0%, reported side effects.

	No. of Patients
Drowsiness	72
Nausea and/or Vomiting	57
Other Gastrointestinal Complaints (Upset Stomach, Heartburn, etc.)	29
Itching, Skin Rash, etc.	15
Vertigo	14
Constipation	6
Miscellaneous	33
	226

for the "sedentary" overeater...

BIPHETAMINE®

A 'STRASIONIC' RELEASE ANORETIC RESIN

BIPHETAMINE '20'
(20 mg.)

BIPHETAMINE '12½'
(12.5 mg.)

BIPHETAMINE '7½'
(7.5 mg.)

Each capsule of each strength contains equal parts of d-amphetamine and dl-amphetamine as cation exchange resin complexes of sulfonated polystyrene.

Single Capsule Daily
Dose 10 to 14 hours
before retiring

PREDICTABLE WEIGHT LOSS

for the "active" overeater...

IONAMIN®

A 'STRASIONIC' ANORETIC PHENYL-*TERT.*-BUTYLAMINE RESIN

IONAMIN '30' (30 mg.) **IONAMIN '15'** (15 mg.)

Each capsule of each strength contains phenyl-*tert.*-butylamine as a cation exchange resin complex of sulfonated polystyrene.

Single Capsule Daily Dose
10 to 14 hours before retiring

STRASENBURGH

NIAMID

brand of nialamide

the mood brightener

...helps her bear chronic disease more cheerfully

When chronic disease is complicated by depression, NIAMID often gives the patient a more cheerful outlook, with improved appetite and increased sense of well-being.

Acting gradually and gently, NIAMID starts improving the attitude of some patients within a few days, and of most other patients within two or three weeks.

An exceptionally well tolerated antidepressant—more than 500,000 prescriptions in many clinical conditions—more than 90 published papers.

NIAMID is supplied as 25 and 100 mg. scored tablets. A Professional Information Booklet is available on request from the Medical Department, Pfizer Laboratories, Brooklyn 6, New York.

Pfizer *Science for the world's well-being™*

orally effective progestational therapy

NORLUTIN®

(norethindrone, Parke-Davis)

in conditions involving deficiency of progesterone...

primary and secondary amenorrhea • menstrual irregularity • functional uterine bleeding • endocrine infertility • habitual abortion • threatened abortion • premenstrual tension • dysmenorrhea

PACKAGING: 5-mg. scored tablets, bottles of 30.

12660

PARKE, DAVIS & COMPANY • ***DETROIT 32, MICHIGAN***

PARKE-DAVIS

to relieve inflammation fast

Seborrheic dermatitis before treatment

clinical photographs

48 hours after treatment

TOPICAL CREAM

NeoDecadron*

DEXAMETHASONE 21-PHOSPHATE—NEOMYCIN SULFATE

mg. for mg. the most active steroid topically optimal concentration for peak effectiveness . . . maximal contact at the site of lesion interrupts the itch-scratch cycle . . . helps maintain patient comfort day and night quick-acting, broad antimicrobial activity no stain, smell, or stickiness

INDICATIONS: Allergic or inflammatory dermatoses, with or without pruritus; sunburn; insect bites; otitis externa (only if the drum is intact).

CAUTION: Steroids should not be used in the presence of tuberculosis of the skin.

DOSAGE: A small quantity of NeoDECADRON Topical Cream (0.1%) is applied to the affected area 2-3 times daily.

SUPPLIED: NeoDECADRON Topical Cream is supplied in 5 Gm. (⅙ oz.) and 15 Gm. (½ oz.) tubes. Each gram contains 1 mg. of dexamethasone 21-phosphate (as disodium salt) and 5 mg. of neomycin sulfate (equivalent to 3.5 mg. neomycin base).

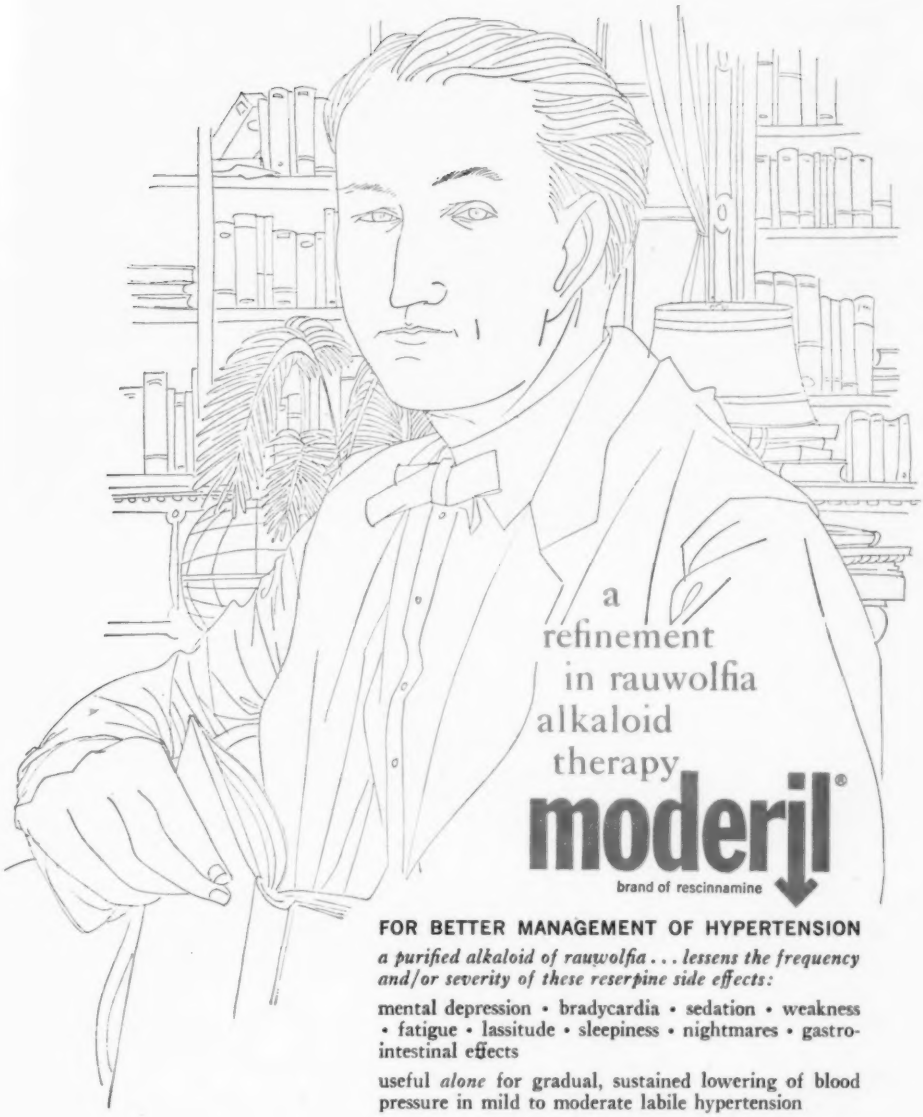
The cream is also available with dexamethasone 21-phosphate only, as DECADRON® Phosphate Topical Cream. Package sizes and steroid concentration are the same as above.

Additional information is available to physicians on request.

*NeoDECADRON and DECADRON are trademarks of Merck & Co., INC.

MSD

MERCK SHARP & DOHME
Division of Merck & Co., INC., West Point, Pa.



a refinement in rauwolfia alkaloid therapy

moderil®

brand of rescinnamine

FOR BETTER MANAGEMENT OF HYPERTENSION

a purified alkaloid of rauwolfia . . . lessens the frequency and/or severity of these reserpine side effects:

mental depression • bradycardia • sedation • weakness • fatigue • lassitude • sleepiness • nightmares • gastrointestinal effects

useful *alone* for gradual, sustained lowering of blood pressure in mild to moderate labile hypertension

useful *as an adjunct* to other types of antihypertensive agents, permitting their use in lower, better tolerated dosage

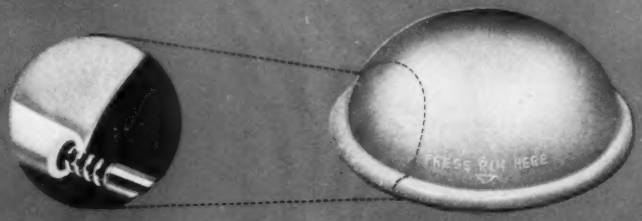
Professional information available on request

PFIZER LABORATORIES Division, Chas. Pfizer & Co., Inc. Brooklyn 6, N.Y. Pfizer *Science for the world's well-being™*

TO FIT YOUR PATIENT...

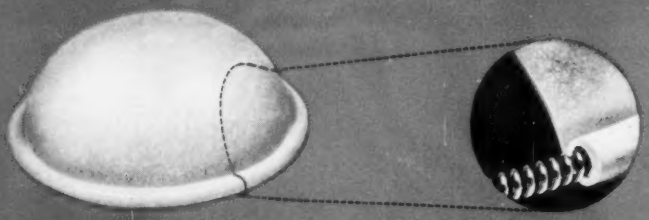
NEW...

ORTHO® Arcing Spring Diaphragm



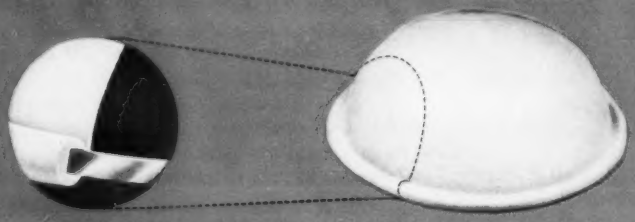
Forms a perfect arc—easy to insert...ideal for the normal and difficult-to-fit patient.

ORTHO® Diaphragm (Coil Spring)



Flexes in all planes—adapts readily to irregular contours of the vagina... assures optimal fit and comfort.

ORTHO®-WHITE Diaphragm (Flat Spring)



Flexes in one plane—inserts easily, needs no introducer... light as a feather and white as snow.

A COMPLETE CHOICE

Ortho

rapid remission of bacterial diarrhea

For superior adsorbent action, POLYMAGMA contains Claysorb which is five times more adsorbent than kaolin. The two antibiotics in POLYMAGMA—polymyxin and dihydrostreptomycin—provide synergistic bactericidal action against common enteric pathogens to help restore normal intestinal function.

POLYMAGMA is unusually safe as systemic absorption of oral polymyxin and dihydrostreptomycin is negligible.

New in vitro study† shows Claysorb is 98-99% effective in adsorbing human enteric viruses Coxsackie, ECHO and poliomyelitis, types 1,2,3. Adsorption is immediate and constant over a wide range of pH and temperature.

Supplied: Bottles of 8 fl. oz. Wyeth Laboratories Philadelphia 1, Pa.

†Bartell, P., Pierzchala, W., and Tint, H.: J. Am. Pharm. A. (Sc. Ed.) *49*:1 (Jan.) 1960.

100 ANNIVERSARY Wyeth

A Century of Service to Medicine

*Trademark

POLYMAGMA®

Polymyxin B Sulfate, Dihydrostreptomycin Sulfate, and Pectin with Claysorb* (Activated Attapulgite, Wyeth) in Alumina Gel, Wyeth

in depression . . . positive and invaluable therapeutic results, but

PLEASE DO NOT PRESCRIBE Catron®

pheniprazine hydrochloride

UNLESS . . . the cautions and provisions for the use of this drug can be consistently applied to the management of your patients. ☐ We make this request now because our surveys indicate that in approximately 50 per cent of patients, prescribed dosage of CATRON is higher than recommended, or prescriptions are not limited to amounts small enough to insure frequent return of the patient for observation. Also, in some instances, therapy was unduly prolonged. ☐ CATRON has displayed outstanding efficacy in depression, angina, and rheumatoid arthritis. But because of the nature of MAO inhibitor therapy, your attention is directed to the extensive and useful instructions prominently displayed in our literature on CATRON, and repeated below.

HOW TO USE CATRON: CATRON is a monoamine oxidase (MAO) inhibitor useful in the treatment of depression and of other disorders indicated below. It is recommended for use in carefully selected cases and in those patients who have not responded to the milder drugs.

ADMINISTRATION AND DOSAGE: Dosage of CATRON must be individualized according to each patient's response. The initial daily dose should not exceed 12 mg. and should be reduced as soon as the desired clinical effect is obtained. A single daily dose in the morning is recommended. A continuous or interrupted schedule may be used, the latter during the maintenance period.

DEPRESSION (Endogenous, Reactive, Postpartum, Involutional, and Depression Secondary to Schizophrenic or Neurotic Reaction): initially, 12 mg. once daily for approximately 2 weeks, or less if improvement appears. Dosage is then reduced to 6 mg. daily. As improvement continues, maintenance dosage of 6 mg. every other day or of 3 mg. daily often proves satisfactory. An interrupted dose schedule is recommended for long-term therapy.

ANGINA PECTORIS: 3 to 6 mg. daily in most cases. Relief of pain and elevation of mood may be dramatic. Victims of angina pectoris who respond in this manner should be cautioned against overexertion induced by their sense of well-being.

RHEUMATOID ARTHRITIS (Adjunctive Therapy—in severely disabling forms, particularly when accompanied by depression): 9 to 12 mg. daily for 3 days, then 6 mg. daily, reducing further to 3 mg. daily on signs of improvement. If a conventional antiarthritic agent is used, lower doses of each are indicated.

CAUTION: Certain circumstances should be watched carefully when using CATRON.

DRUG POTENTIATION—The list of drugs which CATRON potentiates is not yet complete. Hence, caution should be exercised when combining CATRON with any other drugs such as tranquilizers, phenothiazines, the amphetamines, barbiturates, and hypotensive agents.

HYPOTENSIVE EFFECT—Patients receiving CATRON, but especially elderly and hypertensive patients, should be warned about the possibility of orthostatic hypotension during the initial period of higher dosage. In the few instances where this may occur, lowering of the dose will usually permit continuation of therapy.

VISUAL DISTURBANCES—A reversible red-green color defect has been reported in a few patients, chiefly hypertensives, on extended therapy with CATRON. Discontinue the drug if such changes occur. In a few instances, at unusually high dosage, or where the drug was administered following color disturbances, diminished visual acuity occurred which may be partially irreversible.

ANIMALS, NEUROLOGIC SIGNS—In toxicity studies with animals a neurologic syndrome has been observed, characterized by tremors, muscle rigidity and difficulty in locomotion. Animals displaying this visible neurologic syndrome after prolonged **parenteral** administration usually disclosed a neurologic lesion at autopsy. In other animals these visible neurologic symptoms disappeared following cessation of the drug. No lesions were found after oral administration. Although extensive clinical experience has not shown such reactions to be a problem in humans in recommended dosage, should a similar neurologic disturbance occur, the possibility of drug action should be considered.

SIDE EFFECTS—Major side effects requiring cessation of therapy are infrequent. Other side effects—constipation, delay in starting micturition, increased sweating, hyperreflexia, ankle edema, blurring of vision, dryness of the mouth—are usually readily controlled by lowering the dosage. Rash, observed in a few patients, cleared up rapidly upon discontinuing therapy.

WARNING: Although pharmacologic evidence indicates that CATRON has a selectivity for the brain, it, as well as other monoamine oxidase inhibitors, may cause hepatitis. Because of the possibility of this life-threatening hepatitis, and of other effects discussed above, the following recommendations and precautions should be observed. If necessary, the patient should be hospitalized to expedite adherence to this regimen.

The Following Precautions Are Recommended:

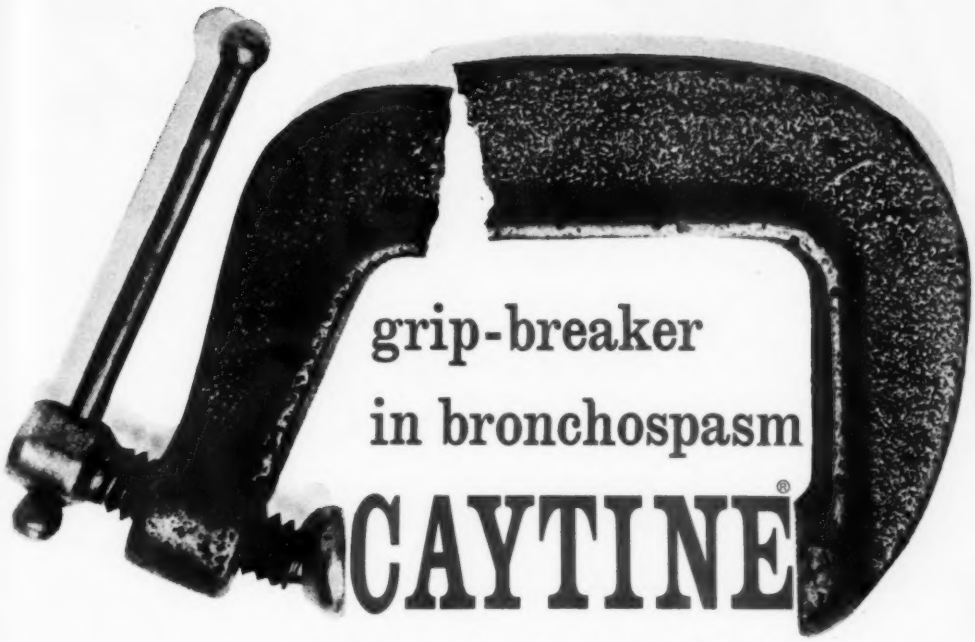
1. Do not use the drug in patients with a history of viral hepatitis or other liver abnormalities.
2. Perform regular liver function tests.
3. In all instances daily dose should not exceed 12 mg.
4. Reduce daily dose as soon as response is established, usually in a matter of 1 to 2 weeks.
5. Do not prescribe to a patient more than sixteen 6 mg. tablets or thirty-two 3 mg. tablets of CATRON at one time.
6. Patient should return for observation before additional CATRON is prescribed. For this reason, prescriptions for CATRON should be marked, "Not refillable."

SUPPLIED: CATRON is the original brand of pheniprazine hydrochloride. It is supplied in tablets of 3 mg. and 6 mg., bottles of 50.

BIBLIOGRAPHY: (1) Agin, H. V.: The Use of JB-516 (CATRON) in Psychiatry, Conference on Amine Oxidase Inhibitors, New York Academy of Sciences, Nov. 20-22, 1958. (2) Bercel, N. A.: Pharmacologic Approach to the Study of the Mind, Springfield, Ill., Charles C Thomas, 1959, p. 331. (3) Kinross-Wright, J.: Panel Discussion of Psychic Energizers, **ibid.** (4) Kinross-Wright, J.: Experience with JB-516 (CATRON) and Other Psychochemicals in Clinical Practice, Conference on Amine Oxidase Inhibitors, New York Academy of Sciences, Nov. 20-22, 1958. (5) Horita, A., and Parker, R. G.: Comparison of Monoamine Oxidase Inhibitory Effects of Iproniazid and Its Phenyl Congener, Proc. Soc. Exper. Biol. & Med. **99**:617, 1958. (6) Horita, A.: Beta-Phenylisopropylhydrazine: A Monoamine Oxidase Inhibitor, Fed. Proc. **17**:379, 1958. (7) Horita, A.: The Pharmacology of the Monoamine Oxidase Inhibitors, in A Pharmacologic Approach to the Study of the Mind, Springfield, Ill., Charles C Thomas, 1959, p. 271. (8) Kennamer, R., and Prinzmetal, M.: Treatment of Angina Pectoris with CATRON (JB-516), Am. J. Cardiol. **3**:542, 1959. (9) Scherbel, A. L., and Harrison, J. W.: The Effects of Iproniazid and Some Other Amine Oxidase Inhibitors in Rheumatoid Arthritis, Conference on Amine Oxidase Inhibitors, New York Academy of Sciences, Nov. 20-22, 1958.

Lakeside Laboratories, Inc • Milwaukee 1, Wisconsin

64950R



grip-breaker in bronchospasm

CAYTINE®

orally, parenterally, and by inhalation

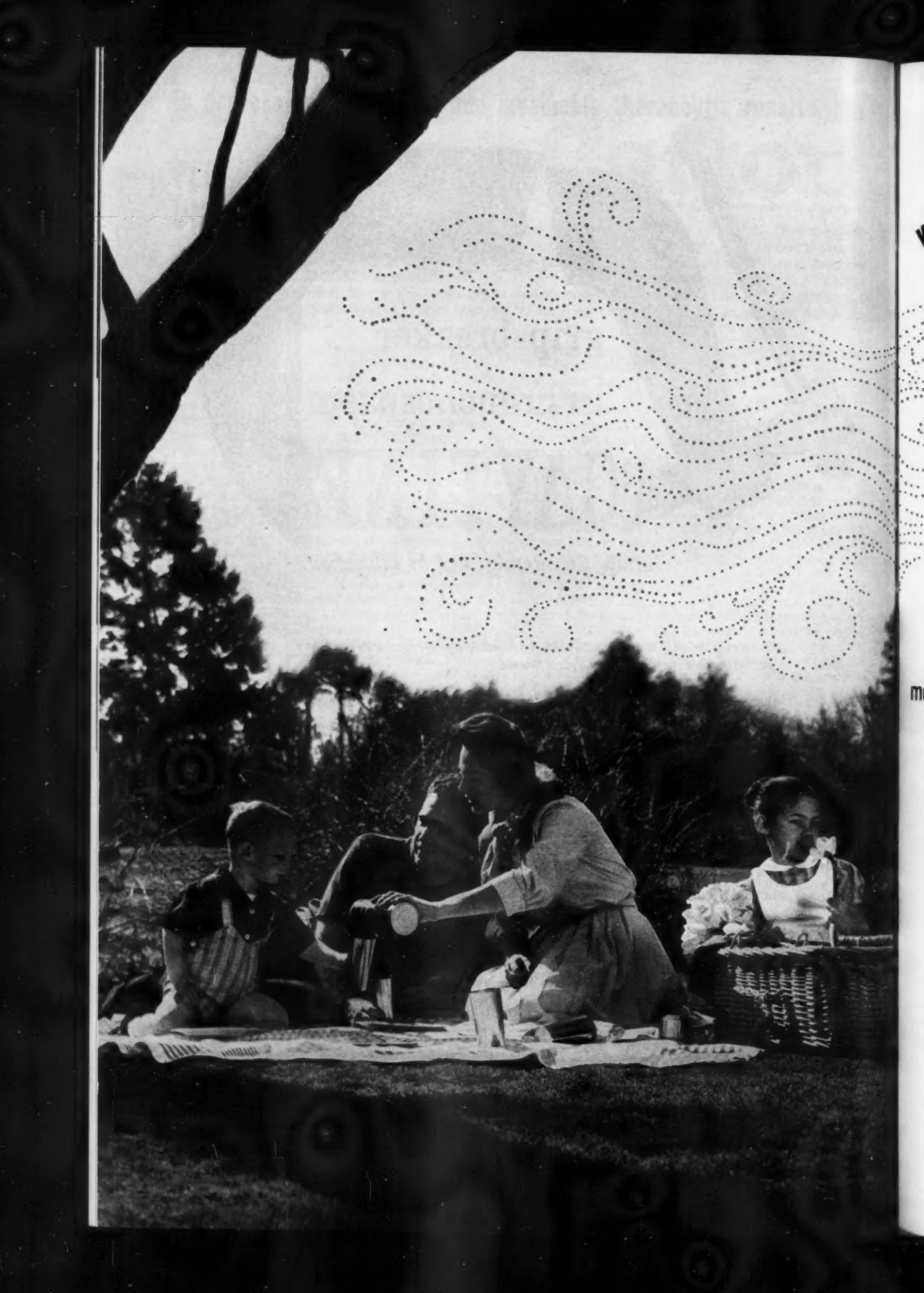
CAYTINE is the only brand of α[(α-methyl-3,4-methylenedioxyphenethylamino)-methyl]-protocatechuyl alcohol hydrochloride.

three forms for individualized management: In patients with asthma, emphysema, bronchitis, bronchiectasis, CAYTINE Tablets, Inhalation, and Injection permit the physician to determine the treatment that gives the greatest relief with fewest side effects. CAYTINE increases vital capacity more than isoproterenol.[1] In geriatric patients, CAYTINE "...was more effective than any previous medication used."[2] There are a few side effects, but no toxic reactions, with the use of CAYTINE. No elevation of blood pressure, no adverse ECG, EEG, hepatic, renal or hematologic changes have been noted. Patients may experience palpitations and anxiety and should be so warned.

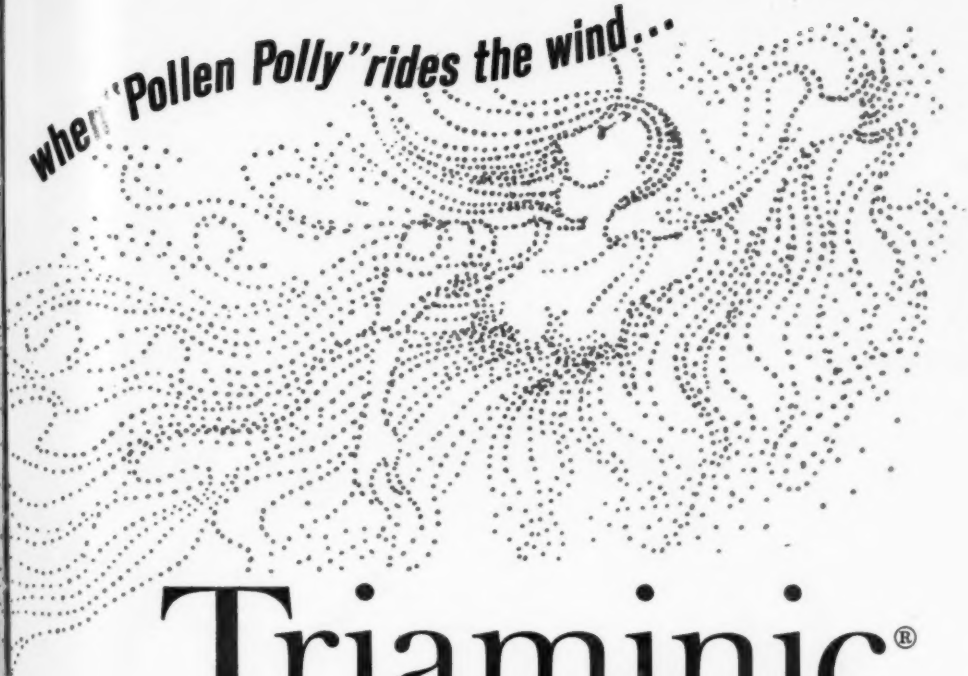
(1) Leslie, A., and Simmons, D. H.: Am. J. M. Sc. *234*:321, 1957. (2) Settel, E.: Am. Pract. & Digest Treat. *8*:1249, 1957.

For additional information request Brochure No. NDA 18, CAYTINE, Lakeside Laboratories, Inc., Milwaukee 1, Wisconsin.

LAKESIDE



when "Pollen Polly" rides the wind...



Triaminic®

...relief from pollen allergies

more complete than antihistamines alone... more thorough than nose drops or sprays

The miseries of respiratory allergy can be relieved so effectively with Triaminic.[1-5] Triaminic contains two antihistamines plus the decongestant, phenylpropanolamine, to help shrink the engorged capillaries, reduce congestion and bring relief from rhinorrhea and sinusitis.[1] Oral administration distributes medication to *all* respiratory membranes without risk of "nose drop addiction" or rebound congestion.[2,3]

Each Triaminic timed-release Tablet provides:

Phenylpropanolamine HCl	50 mg.
Pheniramine maleate	25 mg.
Pyrilamine maleate	25 mg.

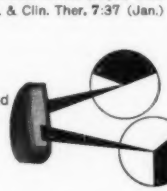
also available:

TRIAMINIC JUVELETS® ½ the formulation of the Triaminic Tablet with timed-release action.

TRIAMINIC SYRUP each teaspoonful (5 ml.) provides ¼ the formulation of the Triaminic Tablet.

References: 1. Fabricant, N.D.: E.E.N.T. Monthly **37**:460 (July) 1958. 2. Lhotka, F. M.: Illinois M.J. **112**:259 (Dec.) 1957. 3. Farmer, D. F.: Clin. Med. **5**:1183 (Sept.) 1958. 4. Fuchs, M.; Bodi, T.; Mallen, S. R.; Hernando, L., and Moyer, J. H.: Antibiotic Med. & Clin. Ther. **7**:37 (Jan.) 1960. 5. Halpern, S. R., and Rabinowitz, H.: Ann. Allergy **18**:36 (Jan.) 1960.

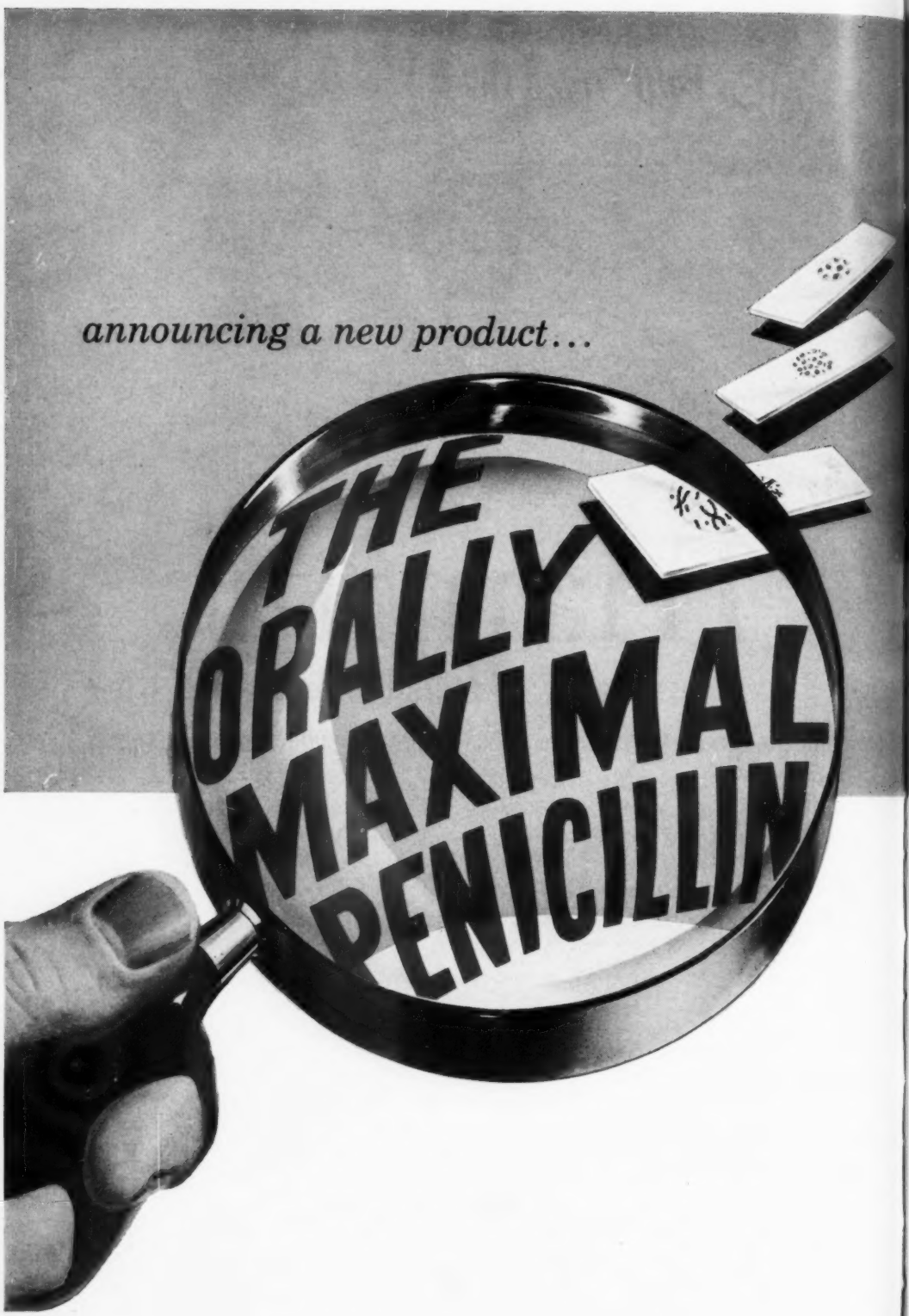
Relief is prompt and prolonged because of this special timed-release action



first—the outer layer dissolves within minutes to produce 3 to 4 hours of relief

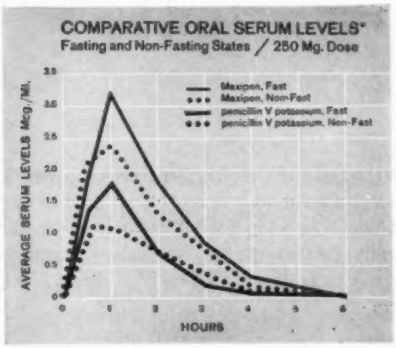
then—the core disintegrates to give 3 to 4 **more** hours of relief

SMITH-DORSEY • A DIVISION OF THE WANDER COMPANY • LINCOLN, NEBRASKA


announcing a new product...
THE
ORALLY
MAXIMAL
PENICILLIN

MAXIMAL ABSORPTION Acid stable, extremely soluble. MAXIPEN is rapidly absorbed from the gastrointestinal tract.

MAXIMAL BLOOD LEVELS Substantially higher than potassium penicillin V (higher levels than with intramuscular procaine penicillin G). You get injection levels with a tablet.



*Based on 3294 individual serum antibiotic determinations. Complete details on request.

MAXIMAL FLEXIBILITY May be administered without regard to meals. However, highest absorption is achieved when taken just before or between meals.

MAXIMAL ORAL INDICATIONS Indicated in infections caused by streptococci, pneumococci, susceptible staphylococci, and gonococci, including:

pneumococcal pneumonia	impetigo
gonorrhea	susceptible staphylococcal abscesses (with indicated surgery)
tonsillitis	
laryngitis	
otitis media	cellulitis
streptococcal pharyngitis	lymphangitis
	pyoderma

Also prophylactically in secondary infections following tonsillectomy, dental extractions, other surgical procedures.

Dosage: For moderately severe conditions, 125 to 250 mg. three times daily. For more severe conditions, 500 mg. as often as every four hours around the clock.

Note: To date, MAXIPEN has not shown less allergic reactions than older oral penicillins. Usual precautions regarding administration should be observed.

Supplied: MAXIPEN TABLETS, scored, 125 mg. (200,000 units) bottles of 36; 250 mg. (400,000 units) bottles of 24 and 100.
MAXIPEN FOR ORAL SOLUTION; reconstituted each 5 cc. contains 125 mg., in 60 cc. bottles.

Triumph of Man Over Molecule
Designed by Pfizer for Maximal Benefit

New York 17, N. Y.
J. B. Roerig and Company
Division, Chas. Pfizer & Co., Inc.
Science for the World's Well-Being™

FOR OUTSTANDING PURITY AND

RUBRAMIN PC

SQUIBB **VITAMIN B_{12}** INJECTION U.S.P.

WHATEVER THE INDICATION FOR B_{12} THERAPY... pernicious anemia • severe nutritional macrocytic anemias • severe nutritional neuropathies • prevention of macrocytic anemia following partial or total gastrectomy • relief of pain in trigeminal neuralgia, osteoarthritis, secondary burning paresthesias, herpes zoster, neuroblastoma in children • when high doses of vitamin B_{12} are required for any condition

SQUIBB *Squibb Quality—the Priceless Ingredient*

"RUBRAMIN" ® IS A SQUIBB TRADEMARK

URITY AND GUARANTEED POTENCY

AMIN PC

PURE CYANOCOBALAMIN INJECTION

POTENCY CONFIRMED! MANY CHEMICAL AND BIOLOGICAL METHODS ARE USED BY SQUIBB TO ASSURE THE QUALITY OF RUBRAMIN PC, INCLUDING THE RADIOISOTOPE DILUTION ASSAY TECHNIQUES

us anemia
hies • pre
• relief of
aresthesias
in B_{12} are

PURE CYANOCOBALAMIN INJECTION RUBRAMIN PC MEETS THE MOST EXACTING STANDARDS OF INTRAVENOUS, INTRAMUSCULAR AND SUBCUTANEOUS ADMINISTRATION

• an original product of Squibb Research—quality confirmed according to the most exacting methods of assay • B_{12} parenteral of choice that may be administered intravenously, intramuscularly, or subcutaneously • virtually painless on injection • remarkably free from side reactions, well-tolerated even when administered in massive doses RUBRAMIN PC is available in 4 different potencies to meet your requirements: 30, 50 and 100 mcg. per cc., 10 cc. vials; 1000 mcg. per cc., 1 cc., 5 cc. and 10 cc. vials.

Proven

in over five years of clinical use and more than 750 published clinical studies

Effective

for relief of anxiety and tension

Outstandingly Safe

- simple dosage schedule produces rapid, reliable tranquilization without unpredictable excitation
- no cumulative effects, thus no need for difficult dosage readjustments
- does not produce ataxia, change in appetite or libido
- does not produce depression, Parkinson-like symptoms, jaundice or agranulocytosis
- does not impair mental efficiency or normal behavior

for the tense and nervous patient

Despite the introduction in recent years of "new and different" tranquilizers, Miltown continues, quietly and steadfastly, to gain in acceptance. Generically and under the various brand names by which it is distributed, meprobamate (Miltown) is prescribed by the medical profession more than any other tranquilizer in the world.

The reasons are not hard to find. Miltown is a *known* drug, evaluated in more than 750 published clinical reports. Its few side effects have been fully reported; there are no surprises in store for either the patient or the physician. It can be relied upon to calm anxiety and tension quickly and predictably.

Usual dosage: One or two 400 mg. tablets t.i.d.
Supplied: 400 mg. scored tablets, 200 mg. sugar-coated tablets; or as MEPROTABS*—400 mg. *unmarked*, coated tablets.

*TRADE-MARK

Miltown®

meprobamate (Wallace)

WALLACE LABORATORIES / *New Brunswick, N. J.*

CM-2063

when that early Monday morning telephone call is from a weekend do-it-yourselfer

"...and this morning, Doctor, my back is so stiff and sore I can hardly move."

now...there is a way to prompt, dependable relief of back distress

the pain goes while *the muscle relaxes*

POTENT – rapid relief in acute conditions

SAFE – for prolonged use in chronic conditions

notable safety – extremely low toxicity; no known contraindications; side effects are rare; drowsiness may occur, usually at higher dosages

rapid action, sustained effect – starts to act quickly, relief lasts up to 6 hours

easy to use – usual adult dosage is one 350 mg. tablet 3 times daily and at bedtime

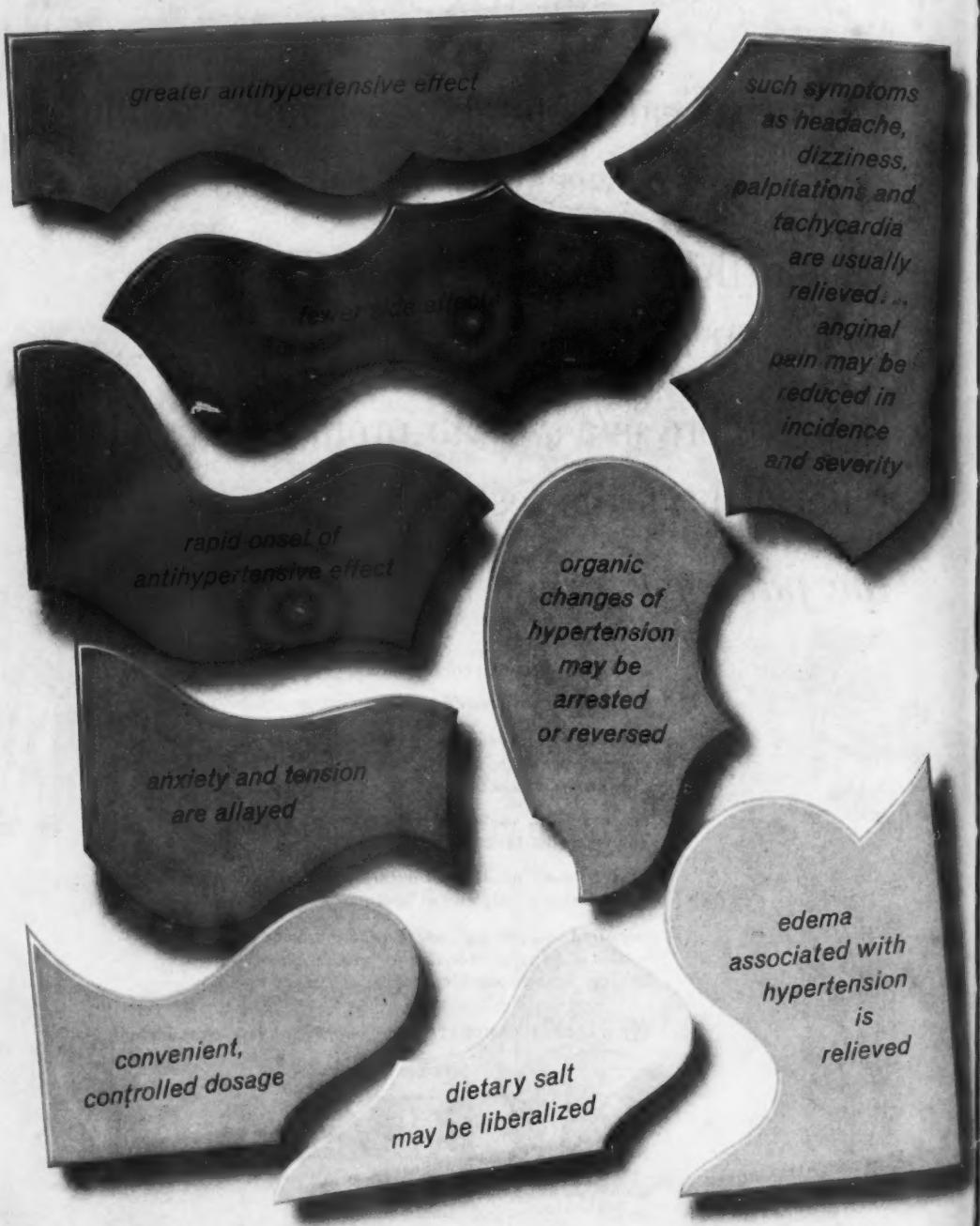
supplied – as 350 mg., white, coated tablets, bottles of 50; *also available for pediatric use:* 250 mg., orange capsules, bottles of 50

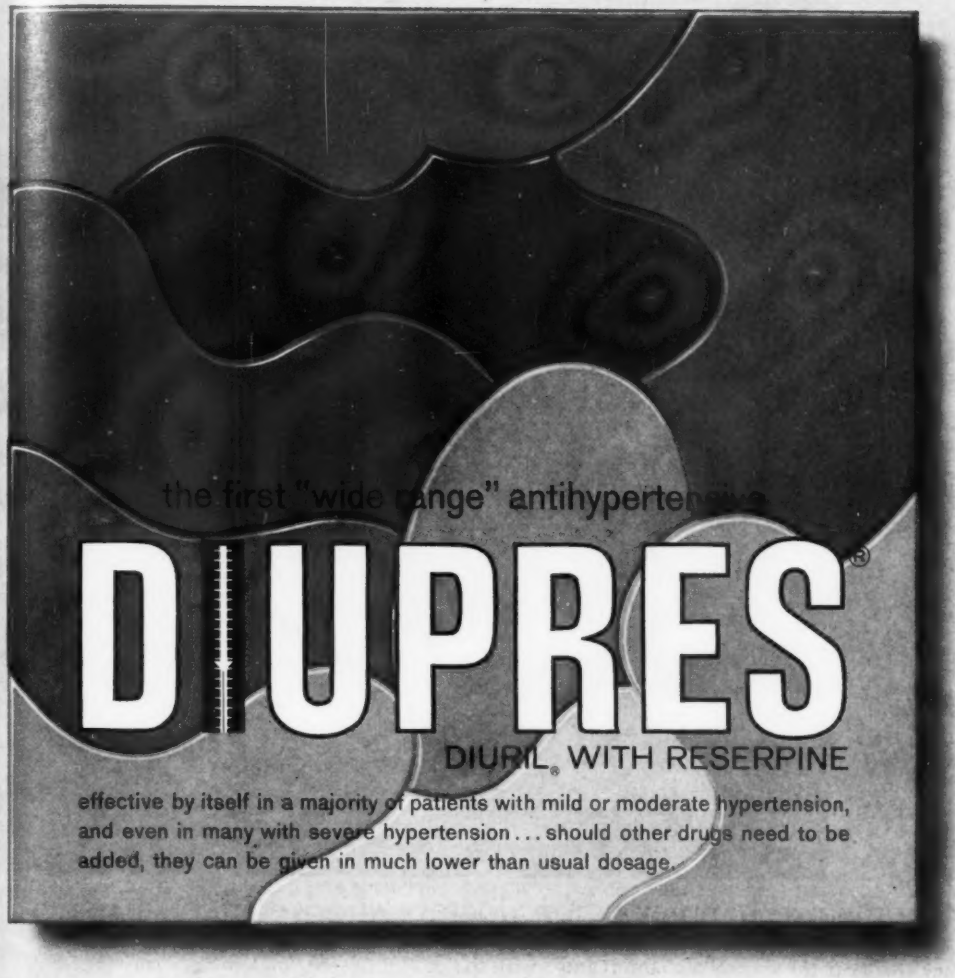
® WALLACE LABORATORIES, New Brunswick, New Jersey

SOMA™

(CARISOPRODOL WALLACE)

here are some of the ways hypertensive patients benefit when you prescribe **DIUPRES**


greater antihypertensive effect
such symptoms as headache, dizziness, palpitations and tachycardia are usually relieved; ... anginal pain may be reduced in incidence and severity
fewer side effects
rapid onset of antihypertensive effect
organic changes of hypertension may be arrested or reversed
anxiety and tension are allayed
edema associated with hypertension is relieved
convenient, controlled dosage
dietary salt may be liberalized


the first "wide range" antihypertensive
DIUPRES®
DIURIL® WITH RESERPINE
effective by itself in a majority of patients with mild or moderate hypertension, and even in many with severe hypertension . . . should other drugs need to be added, they can be given in much lower than usual dosage.

DIUPRES-250

250 mg. DIURIL (chlorothiazide),
0.125 mg. reserpine per tablet.
One tablet one to four times a day.

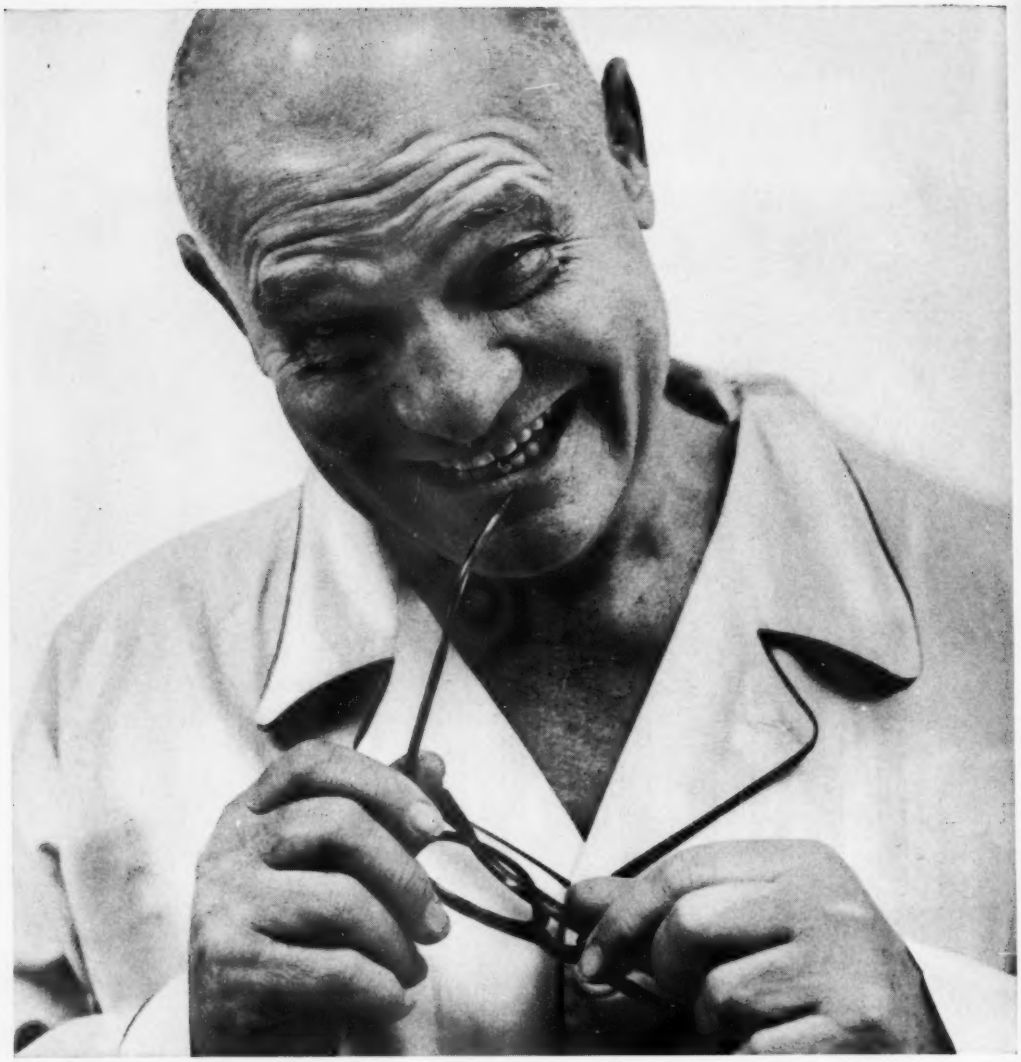
DIUPRES-500

500 mg. DIURIL (chlorothiazide),
0.125 mg. reserpine per tablet.
One tablet one to three times a day.

For additional information, write Professional Services, Merck Sharp & Dohme, West Point, Pa.

DIUPRES and DIURIL are trademarks of Merck & Co., Inc.

MERCK SHARP & DOHME, DIVISION OF MERCK & CO., INC., PHILADELPHIA 1, PA.



Patients are happier when doctors choose Fleet® Enema

They are free of the visceral discomfort and prolonged embarrassment so often caused by older enema methods. The ready-to-use Fleet Enema squeeze bottle also does away with troublesome preparation and cleanup procedures. Insertion is made easy and safe with the pre-lubricated, anatomically correct 2-inch rectal tube. Most important—Fleet Enema provides a quick yet thorough cleansing action with only 4½ fl.oz. of precisely formulated, standardized solution.[1]

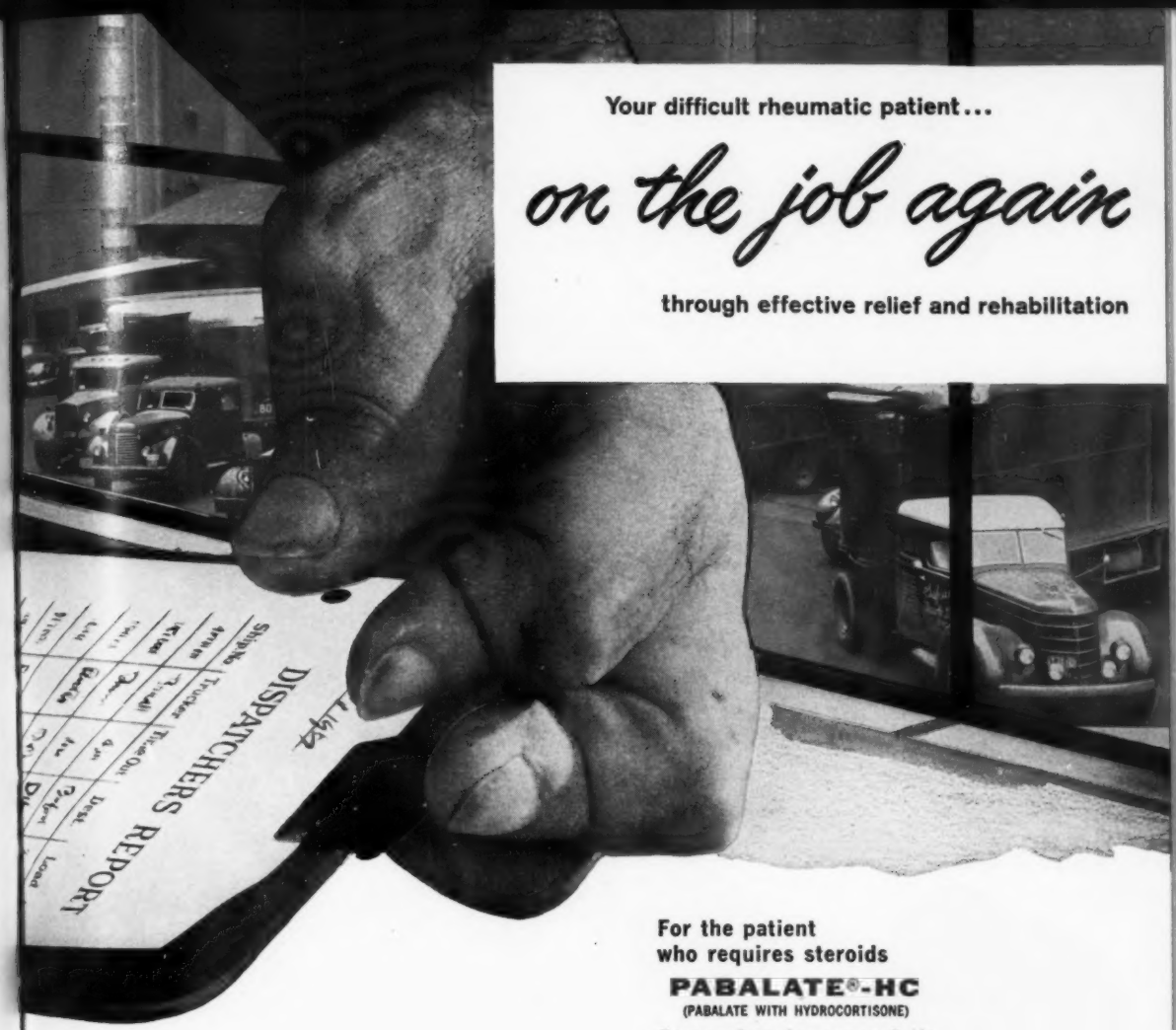
You can order Fleet Enema with confidence for a variety of diagnostic and therapeutic purposes—even for patients on sodium-restricted regimens.[2] Systemic absorption is negligible.

100 cc. contains: 16 Gm. sodium biphosphate and 6 Gm. sodium phosphate in 4¼-fl.oz. squeeze bottle. *Pediatric size,* 2¼ fl.oz. *Also available:* Fleet Oil Retention Enema, 4¼-fl.oz. ready-to-use unit containing Mineral Oil U.S.P.

Fleet FLEET® ENEMA
READY-TO-USE SQUEEZE BOTTLE

1. Rosenfield, H. H., et al.: Obst. & Gynec. 11:222, 1958. 2. Hellman, L. D.: To be published.

C. B. FLEET CO., INC. LYNCHBURG, VIRGINIA



Your difficult rheumatic patient...

on the job again

through effective relief and rehabilitation

For the patient who does not require steroids

PABALATE®

Reciprocally acting nonsteroid antirheumatics . . . more effective than salicylate alone.

In each enteric-coated tablet:

Sodium salicylate U.S.P.....0.3 Gm. (5 gr.)
Sodium para-aminobenzoate .....0.3 Gm. (5 gr.
Ascorbic acid .....50.0 mg

or for the patient who should avoid sodium

PABALATE® - Sodium Free

Pabalate, with sodium salts replaced by potassium salts.

In each enteric-coated tablet:

Potassium salicylate .....0.3 Gm. (5 gr.)
Potassium para-aminobenzoate .....0.3 Gm. (5 gr.)
Ascorbic acid .....50.0 mg.

For the patient who requires steroids

PABALATE®-HC

(PABALATE WITH HYDROCORTISONE)

Comprehensive synergistic combination of steroid and nonsteroid antirheumatics... full hormone effects on low hormone dosage . . . satisfactory remission of rheumatic symptoms in 85% of patients tested.

In each enteric-coated tablet:

Hydrocortisone (alcohol) ..... 2.5 mg.
Potassium salicylate ..... 0.3 Gm.
Potassium para-aminobenzoate.. 0.3 Gm.
Ascorbic acid .....50.0 mg.

PABALATE® Robins PABALATE®-HC

For steroid or non-steroid therapy: SAFE DEPENDABLE ECONOMICAL

A. H. ROBINS CO., INC., RICHMOND 20, VIRGINIA • Ethical Pharmaceuticals of Merit since 1878

THE CLINICAL STUDY[1]: Treatment of obesity.

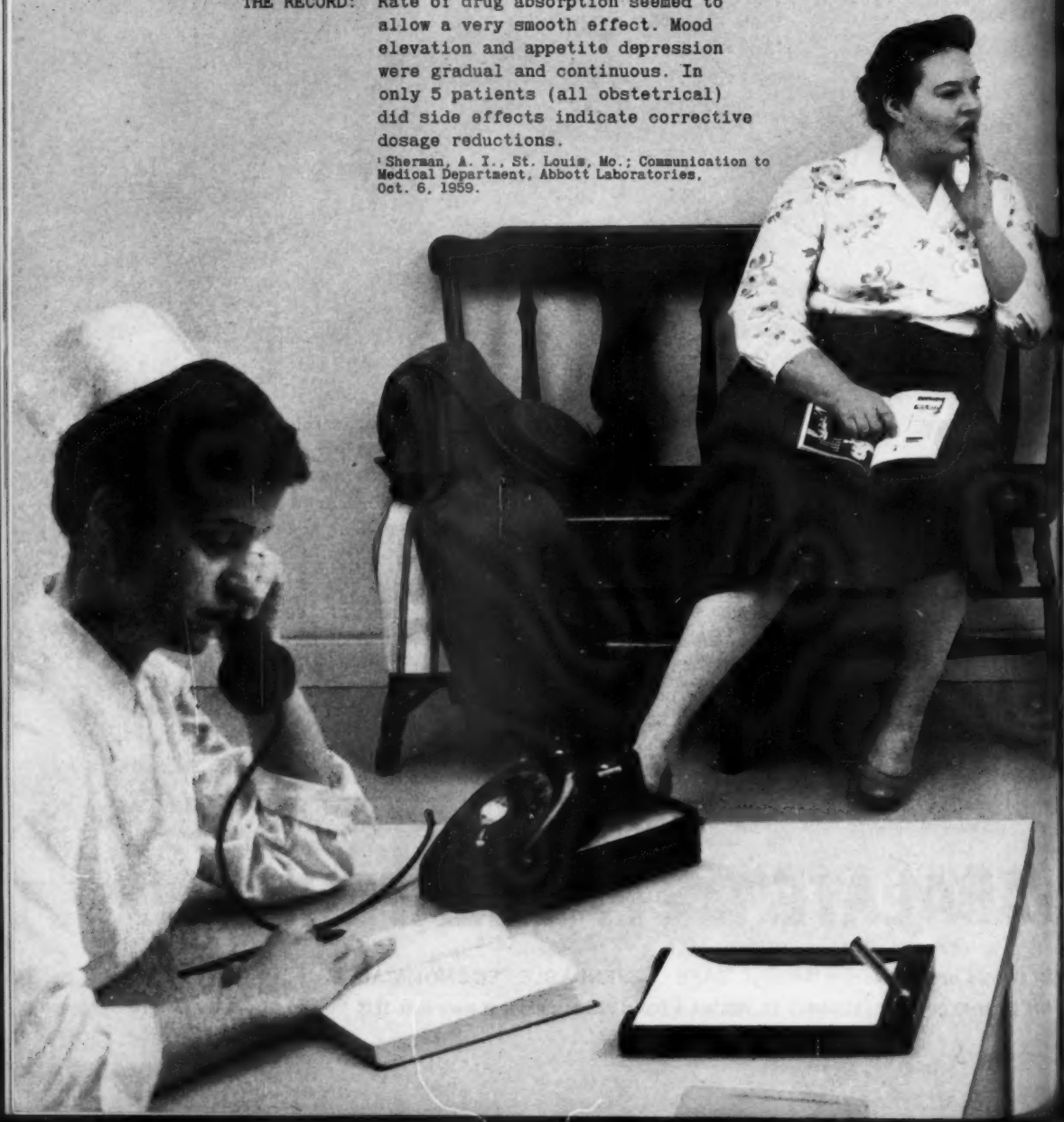
THE PATIENTS: 73 patients—26 obstetrical, 47 non-obstetrical—all of whom had previously dieted unsuccessfully.

THE DOSAGE: 5, 10 or 15 mg., orally, once daily, in the morning.

THE RESULTS: Average weight loss of 20.8 lbs. in non-obstetrical patients treated from 5½ to 30 weeks; average loss of 23.6 lbs. in obstetrical patients (postpartum) treated from 8 to 42 weeks. All patients lost weight.

THE RECORD: Rate of drug absorption seemed to allow a very smooth effect. Mood elevation and appetite depression were gradual and continuous. In only 5 patients (all obstetrical) did side effects indicate corrective dosage reductions.

[1] Sherman, A. I., St. Louis, Mo.; Communication to Medical Department, Abbott Laboratories, Oct. 6, 1959.



NEW INDICATION

relieves
menstrual
cramps...
by
relaxing
uterine
spasm

myo- -vascular relaxant

VASODILAN®

Isoxsuprine hydrochloride, Mead Johnson

relieves menstrual cramps through non-hormonal action on uterine muscle

- does not disturb normal menstrual rhythm or flow
- is well tolerated in recommended oral doses
- can be used safely with other drugs

reports of clinical effectiveness

In the laboratory...relieves spasm of uterine muscle[1,2] and in clinical studies...relieves cramps in approximately 86 per cent of patients.[2,3]

dosage and administration for menstrual cramps: 10 to 20 mg. (1 or 2 tablets) three or four times daily, begun 24 to 72 hours prior to the expected onset of menstruation and continued until pain has been averted. If pain has already started, initial therapy should be 20 mg. (2 tablets) repeated three or four times daily. For full details, see brochure available on request from Mead Johnson & Company, Evansville 21, Indiana.

Supplied: 10 mg. tablets, and 2 cc. ampuls containing 10 mg. (5 mg./cc.) *for intramuscular use.*

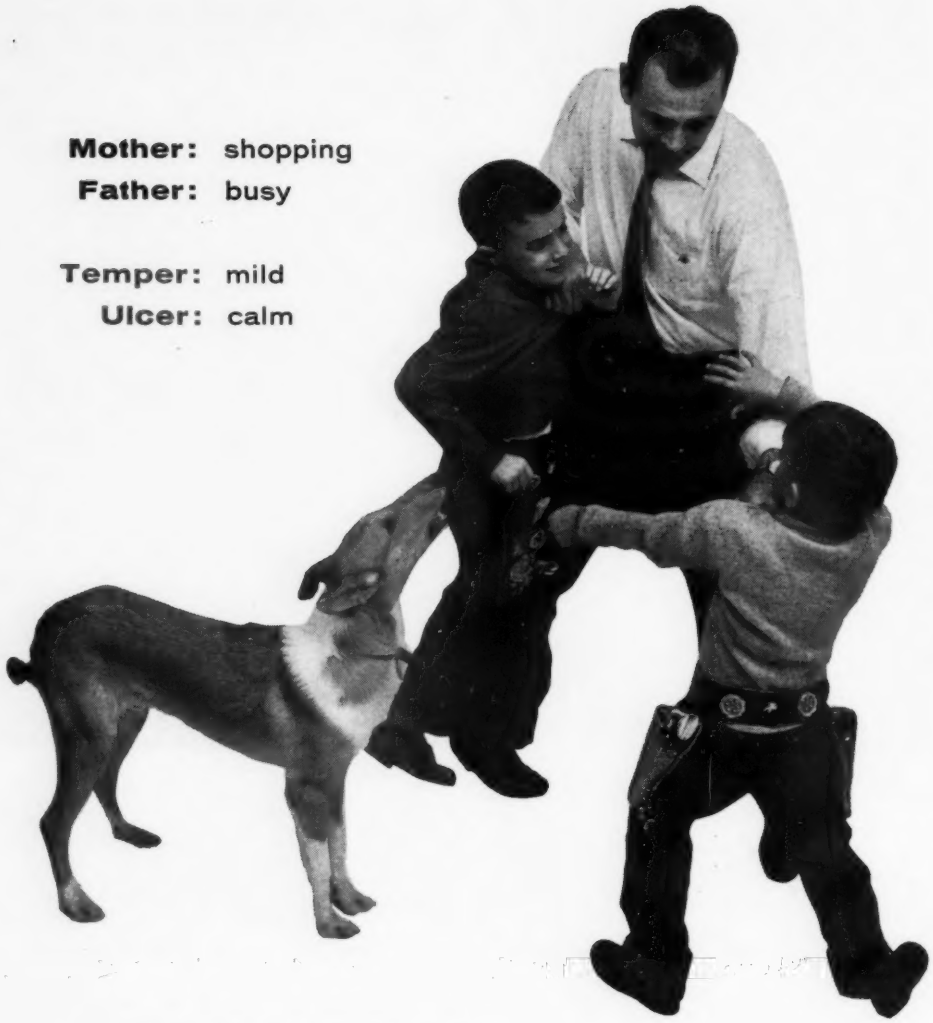
References: (1) Voulgaris, D. M.: Dysmenorrhea: Cramps or Psyche?, Scientific Exhibit, 108th Ann. Meet., Atlantic City, June 8-12, 1959. (2) Detailed reports in Mead Johnson research files. (3) Voulgaris, D. M.: Obst. & Gynec. *15*: 220-222 (Feb.) 1960.

Mead Johnson
Symbol of service in medicine

88869

Mother: shopping
Father: busy

Temper: mild
Ulcer: calm



His ulcer should be protesting—he remains calm. His physician has prescribed ALUDROX SA because he knows *the patient as well as the ulcer must be treated.*

• calms emotional distress • promotes healing • reduces acid secretion • relieves pain • inhibits gastric motility

ALUDROX® SA

Suspension and Tablets: Aluminum Hydroxide Gel with Magnesium Hydroxide, Ambutonium Bromide and Butabarbital, Wyeth

Wyeth Laboratories Philadelphia 1, Pa.

100 ANNIVERSARY Wyeth®

A Century of Service to Medicine

The Wm. S. Merrell Company
announces the availability of

MER/29

(brand of triparanol)

... the first cholesterol-lowering agent to inhibit the formation of excess cholesterol within the body, reducing both serum and tissue cholesterol levels.

... no demonstrable interference with other vital biochemical processes reported to date.

... convenient dosage: one capsule daily.

... toleration and absence of toxicity established by 2 years of clinical investigation.

The following pages report the clinical findings of therapy with MER/29 among patients with hypercholesterolemia and conditions thought to be associated with it, such as

coronary artery disease (angina pectoris, postmyocardial infarction)

generalized atherosclerosis

THE FACTS ABOUT MER/29[1-41]

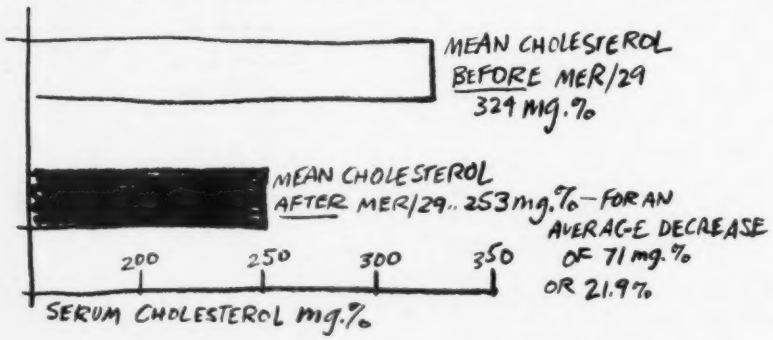
Fundamental differences between MER/29 and other cholesterol-lowering substances

Cholesterol produced within the body—its biosynthesis—is about three times as great as that obtained from dietary sources. Before MER/29, no method of modifying total body cholesterol production was known. Those measures used to lower cholesterol (unsaturated fatty acids or other dietary measures, vitamins, plant sterols, hormones, etc.) succeeded only in modifying exogenous sources of cholesterol or accelerating its metabolism.

MER/29 is fundamentally different, since it inhibits cholesterol biosynthesis. Thus, MER/29 offers for the first time a method of controlling total body cholesterol content.

MER/29 reduces serum cholesterol in 89% of patients, with or without dietary restrictions. Radioisotope studies indicate reduction of tissue cholesterol as well.[4, 5, 7, 30, 31, 34]

High cholesterol levels are generally considered those above 250 mg. %. Here is a tabular summary of preliminary data on MER/29 therapy in 463 patients with hypercholesterolemia (over 250 mg. %).



Clinical studies show that cholesterol reduction usually begins within two weeks. Maximum effect is achieved in five to eight weeks, and is maintained as long as therapy is continued. The studies of Hollander, Chobanian and Wilkins and those of Kountz found that cholesterol levels were lowered by MER/29 therapy irrespective of diet.

Reduction of total body "miscible pool" of cholesterol has been confirmed by radioisotope studies. Hollander and Chobanian, for example, found that the apparent miscible pool of cholesterol was reduced from 184 Gm. in the control period to 100 Gm. during MER/29 administration.

Studies in animals on MER/29 have shown the following tissue changes: erythrocyte cholesterol levels reduced 40%; plasma cholesterol reduced 62%; liver reduced 40%; skeletal muscle reduced 27%; lung reduced 33%; aorta reduced 21%. Significantly, brain and adipose tissue remained unaffected during the period of observation.

Safety and toxicity studies[5, 7, 10, 12, 17, 19, 21-24, 30, 32-34]

MER/29 is well tolerated. In a recent analysis of 576 individual case reports, 165 had been treated with MER/29 for continuous periods in excess of a year. A number had received two to four times the daily recommended dose for as long as 16 months. Side effects were seldom seen, and the incidence of those reported (nausea, dermatitis) was too low for positive correlation with administration of the drug.

In no case has there been clinical indication of toxic effects on the function of any vital organ or system. It should be noted that excretion of MER/29 or its metabolites may produce a false positive reaction for albuminuria.

THE FACTS ABOUT MER/29

Clinical observations of MER/29 in atherosclerosis[5, 7, 10, 12, 17-19, 21, 23-25, 28-34, 41]

The lowering of high cholesterol levels is regarded by many as a desirable clinical objective. Moreover, a substantial body of medical opinion implicates elevated cholesterol as a contributor to coronary artery disease and generalized atherosclerosis. Since MER/29 lowers total body cholesterol, can it modify atherosclerotic conditions? While the ultimate answer must await the results of long-term clinical experience, preliminary observations were reported at...

The MER/29 Conference at Princeton

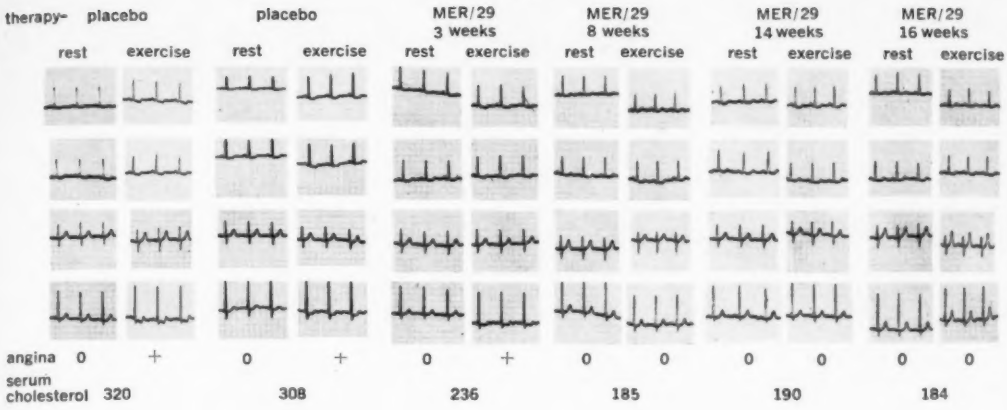
To help find the answer, 18 leading research teams met to discuss the relationship of MER/29 to cholesterol metabolism and atherosclerosis. The conference, moderated by Dr. Irving S. Wright, and summarized by Dr. Konrad E. Bloch, Dr. Robert W. Wilkins, and Dr. Irvine H. Page, was held last December at Princeton, New Jersey.

(The complete transcript of this conference is published as a supplement to the May, 1960, issue of Progress in Cardiovascular Diseases.)

Objective findings

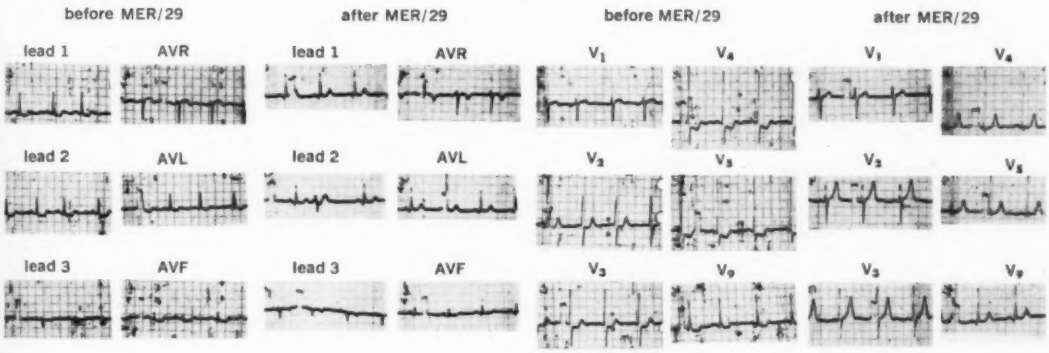
The team of Dr. William Hollander, Dr. Aram V. Chobanian, and Dr. Robert W. Wilkins at Massachusetts Memorial Hospitals, presented Fig. 1. It indicates a reversal of exercise-precipitated ECG abnormalities in a patient with angina pectoris during four months of MER/29 therapy. In all, they reported that three of nine patients showed reversal of exercise-induced ECG abnormalities after three months of MER/29 therapy.

fig. 1


therapy- placebo
placebo
MER/29 3 weeks
MER/29 8 weeks
MER/29 14 weeks
MER/29 16 weeks
rest exercise rest exercise rest exercise rest exercise rest exercise rest exercise
angina 0 + 0 + 0 + 0 0 0 0 0 0
serum cholesterol 320 308 236 185 190 184

Dr. Philip Lisan of Dr. John H. Moyer's group at Hahnemann Hospital presented Fig. 2. It also indicates reversal of ECG abnormalities in a patient with angina pectoris.

fig. 2



Dr. A. C. Corcoran of St. Vincent Charity Hospital, Cleveland, and Dr. Arthur Ruskin of University of Texas reported similar objective findings. All of these investigators noted that patients offered subjective evidence that they were experiencing a feeling of better health on MER/29 therapy, and that nitroglycerine dependence was diminishing.

Negative data were presented by Dr. Henry I. Russek of Staten Island, N. Y. He reported a study of exercise-electrocardiographic tests in 14 selected

subjects on MER/29. None of these patients had shown more than transient improvement in exercise tolerance after 3 months of treatment. It should perhaps be noted that this group of angina pectoris patients were a select group, having complained of symptoms for long periods of time.

Subjective findings

Dr. Meyer P. Halperin of Lynn, Massachusetts, reported a series of 18 patients with angina pectoris. Nine of this group obtained unequivocal subjective relief of symptoms after various periods of therapy with MER/29. An analysis of the duration of symptomatology in these patients indicated that response occurred more frequently when the ischemic heart disease had been present for shorter periods. Specifically, those who responded had had the condition for an average of 2.9 years, while the average time for those who did not respond was 5.2 years.

This study suggests that improvement in angina pectoris, when it occurs, may best be expected in those patients in whom the symptoms have been present for shorter periods of time. Additional experience will be required to determine whether long-term therapy can reverse long-standing symptomatology.

Dr. William B. Kountz of the Washington University School of Medicine, St. Louis, reported a group of 79 patients with varying degrees of hypertension, angina pectoris, diabetes, atherosclerosis or myocardial infarction. "Clinical improvement was observed and was also reported to us by patients. In some instances the anginal pain improved very much."

Similar subjective findings were also reported by

Dr. Corcoran, eight of whose nine patients noted a feeling of better health and increased exercise tolerance on MER/29. In three of these patients, nitroglycerine requirements were dramatically reduced.

IN SUMMARY ... MER/29 does consistently lower total body cholesterol by inhibition of endogenous cholesterol formation. Some patients with coronary artery disease, while on MER/29, have experienced concurrent clinical benefits such as reduction in frequency and severity of anginal attacks, reduction in nitroglycerine dependence, reversal of ECG abnormalities both at rest and following exercise-tolerance-induced changes, and an improved sense of good health and well-being.

The explanation of these clinical benefits is as yet unknown; however, several hypotheses have been advanced. One group speculates that MER/29 "may actually improve the adequacy of coronary circulation." Another investigator suggests that MER/29 exerts a vasodilating action, though pharmacologically MER/29 produces only transient vasodilating effects. Whatever the explanation, observation of these benefits among certain patients has awakened mounting interest in MER/29 as an important new agent in the management of patients with hypercholesterolemia and atherosclerosis.

MER/29 may be given to your patients with hypercholesterolemia and conditions thought to be associated with elevated cholesterol levels, including coronary artery disease (angina pectoris and postmyocardial infarction), and generalized atherosclerosis.

The Wm. S. Merrell Company
announces the availability of

MER/29

(brand of triparanol)

... the first cholesterol-lowering agent to inhibit the formation of excess cholesterol within the body, reducing both serum and tissue cholesterol levels.

Indications: May be used for patients with hypercholesterolemia and conditions thought to be associated with abnormal cholesterol metabolism. These include: coronary artery disease (angina pectoris and postmyocardial infarction), generalized atherosclerosis.

Caution: MER/29 is a new drug which inhibits cholesterol biosynthesis in the body. Since cholesterol plays an important role in the development of the fetus, the drug should not be administered during pregnancy.

Hypercholesterolemia and its associated conditions may require MER/29 therapy over a long period. MER/29 has been shown to be entirely safe in the periods the drug has been studied, but long-term or lifetime effects are unknown. Periodic examination of patients on long-term MER/29 therapy is therefore necessary. While clinical liver damage has not been encountered, periodic liver function tests may be desirable until more long-term safety data are available.

Note: The specific site of action of MER/29 is now known to be between desmosterol (reported to be the last precursor in the synthesis path) and cholesterol. Although greater than normal quantities of desmosterol can be qualitatively shown in the livers and blood of animals and the blood of human beings treated with MER/29, reduction of total sterols suggests little, if any, accumulation. The significance of the presence of this substance is unknown and speculative.

Compatible with other cardiovascular therapies: MER/29 is not to be considered a substitute for measures ordinarily employed to control anxiety, hypertension, obesity, and other conditions associated with cardiovascular disorders. However, MER/29 is compatible with measures used in these disorders, including anticoagulants, nitroglycerine, and PETN.

Dosage: One capsule daily, before breakfast. Each capsule contains 250 mg. triparanol.

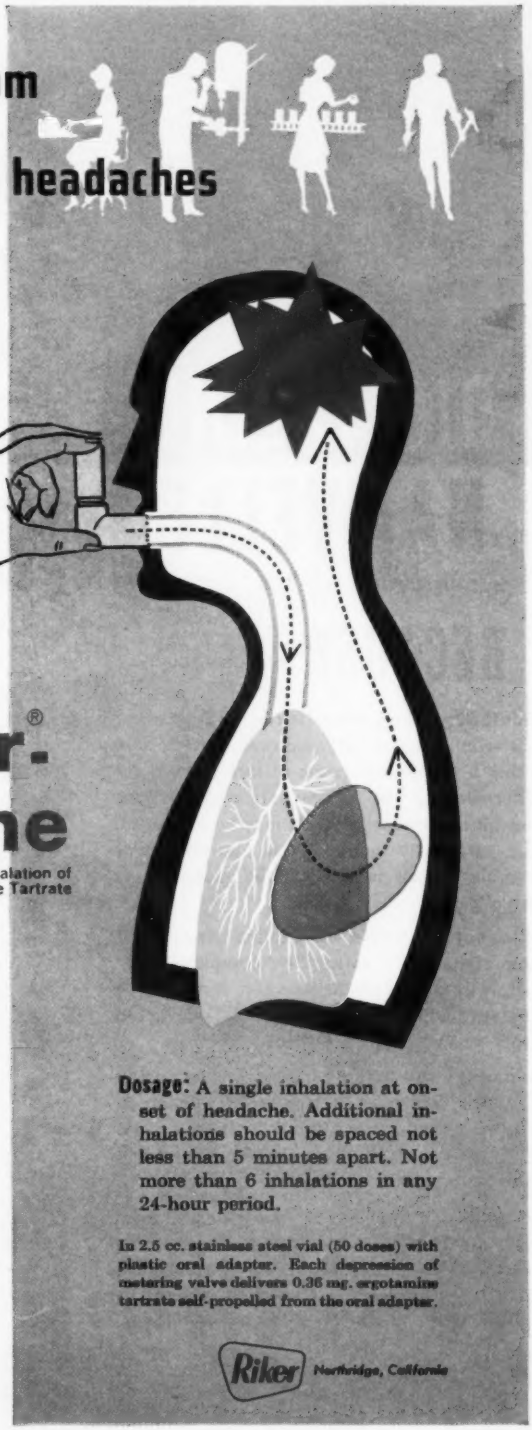
Supplied: In bottles of 30 pearl gray capsules.

References: 1. Blohm, T. R.; Kariya, T.; Laughlin, M. W., and Palopoli, F. P.: Fed. Proc. 18:369, 1959. 2. MacKenzie, R. D., and Blohm, T. R.: Fed. Proc. 18:417, 1959. 3. Van Maanen, E. F.; Blohm, T. R.; Kuhn, W. L.; Greslin, J. G.; Smith, J. K.; Lerner, L. J., and Holtkamp, D. E.: Fed. Proc. 18:454, 1959. 4. Oaks, W., and Lisan, P.: Fed. Proc. 18:428, 1959. 5. Hollander, W., and Chobanian, A.: Boston M. Quart. 10:37, 1959. 6. Blohm, T. R.; Kariya, T., and Laughlin, M. W.: Arch. Biochem. 85:250, 1959. 7. Oaks, W.; Lisan, P., and Moyer, J. H.: A.M.A. Arch. Int. Med. 104:527, 1959. 8. Blohm, T. R., and MacKenzie, R. D.: Arch. Biochem. 85:245, 1959. 9. Palopoli, F. P.: Proc., Conference on MER/29, Progr. Cardiovascular Dis. 2:489 (May) 1960. 10. Gould, R. G.: Ibid., p. 492. 11. King, W.: Ibid., p. 504. 12. Frantz, I. D., Jr.; Mobberley, H. L., and Schroepfer, G. J., Jr.: Ibid., p. 511. 13. Blohm, T. R.; Kariya, T., and MacKenzie, R. D.: Ibid., p. 519. 14. Avigan, J., et al.: Ibid., p. 525. 15. Portman, O. W.; Mayer, J., and Hegsted, D. M.: Ibid., p. 531. 16. Bloch, K. E.: Ibid., p. 539. 17. Kountz, W. B.: Ibid., p. 541. 18. Toro, J.: Ibid., p. 544. 19. Ford, R. V.: Ibid., p. 548. 20. McDevitt, E.: Ibid., p. 553. 21. Todd, M. E.: Ibid., p. 555. 22. Estes, J. E.: Ibid., p. 564. 23. Leckert, J. T., et al.: Ibid., p. 571. 24. Corcoran, A. C.; Zimmerman, H. A., and Cuturelli, R.: Ibid., p. 576. 25. Russek, H. I.: Ibid., p. 578. 26. Steinberg, D., and Feigelson, E. B.: Ibid., p. 586. 27. Wilkins, R. W.: Ibid., p. 593. 28. Waddell, W. R.: Ibid., p. 597. 29. Rosenman, R. H., and Friedman, M.: Ibid., p. 605. 30. Oaks, W. W.: Ibid., p. 612. 31. Lisan, P.: Ibid., p. 618. 32. Ruskin, A., and Ruskin, B.: Ibid., p. 624. 33. Halperin, M. H.: Ibid., p. 631. 34. Hollander, W.; Chobanian, A. V., and Wilkins, R. W.: Ibid., p. 637. 35. Page, I. H.: Ibid., p. 646. 36. Avigan, J., et al.: Fed. Proc. 19:239, 1960. 37. Schroepfer, G. J., Jr.: Fed. Proc. 19:240, 1960. 38. Kariya, T., and Blohm, T. R.: Fed. Proc, 19:14, 1960. 39. MacKenzie, R. D., and Blohm, T. R.: Fed. Proc. 19:14, 1960. 40. King, W. M., and Smith, J. K.: Fed. Proc. 19:14, 1960. 41. Oaks, W.; Lisan, P., and Moyer, J. H.: M. Times 88:593, 1960.

THE WM. S. MERRELL COMPANY Cincinnati, Ohio • St. Thomas, Ont. Merrell

on-the-go relief from recurrent throbbing headaches

including migraine syndromes, other vascular headaches, histaminic cephalalgia, and occipital neuralgia



Medihaler®-Ergotamine

Oral Inhalation of Micronized Ergotamine Tartrate

Fastest overall method for relieving recurrent throbbing headache

Approximates speed and predictability of relief following ergotamine injection.

Eliminates delay in treatment...Medihaler travels *with* the patient...ready and in use in 5 seconds!

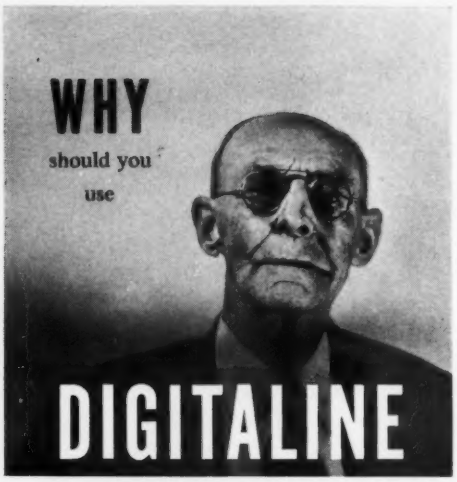
"In a series of over 300 episodes of vascular headache in 41 patients 'Medihaler'-Ergotamine was effective in about 70%."

Graham, J.R.: Faulkner Hospital, Jamaica Plains, Boston.

Dosage: A single inhalation at onset of headache. Additional inhalations should be spaced not less than 5 minutes apart. Not more than 6 inhalations in any 24-hour period.

In 2.5 cc. stainless steel vial (50 doses) with plastic oral adapter. Each depression of metering valve delivers 0.36 mg. ergotamine tartrate self-propelled from the oral adapter.

Riker Northridge, California



NATIVELLE®

the original crystalline digitoxin

BECAUSE it assures you of . . .

Flexibility of Administration—Digitaline Nativelle provides for rapid oral digitalization within a convenient range of tablet strengths. When desired the intravenous route, or the new intramuscular injection may be employed. The essentially non-alcoholic intramuscular formula, unlike most alcoholic menstrua, is virtually painless.

Efficiency of Action—Digitaline Nativelle is pure digitoxin. It is rapidly, completely and uniformly absorbed—neither too fast nor too slow—providing a steady and predictable action upon the heart muscle.

Dependability of Performance—Digitaline Nativelle [digitoxin] is the pure active glycoside insuring optimum range of cardiotonic activity. Digitoxin is a drug of choice when a purified digitalis product is desired.

Adequate Margin of Safety—Digitaline Nativelle provides virtual freedom from annoying local side effects which may occur with the galenicals, and its margin of safety is unexcelled by any other purified preparation. A product of Nativelle, Inc.

E. Fougera & Co., Inc.

FOUGERA

Hicksville, Long Island, N. Y.

Products by Therapy Indications

PHARMACEUTICALS

Analgesics and Narcotics

A.P.C. with Demerol—Winthrop A-2
Dilaudid—Knoll A-179
Medihaler-Ergotamine—Riker A-133
Mepergan—Wyeth A-160
Numorphan—Endo A-191
Oxaine—Wyeth A-70-71
Zactirin—Wyeth A-29

Antacids and Intestinal Adsorbents

Aludrox SA—Wyeth A-132
Gelusil—Warner-Chilcott A-145
Kolantyl—Merrell A-84

Antiallergics

Anergex—Mulford Colloid A-91
Dimetane—Robins A-12
Tacaryl—Mead Johnson ..... Facing A-48-49; A-49
Triaminic—Smith-Dorsey A-110-111

Antibacterials

Furadantin—Eaton A-170-171
Madribon—Roche A-194-195

Antibiotics

Alpen—Schering A-36-37-38-39
Chloromycetin—Parke-Davis A-162-163
Declomycin—Lederle A-212
Dramcillin—White A-130
Humatin—Parke-Davis A-182-183
Maxipen—Roerig A-112-113
Mysteclin-V—Squibb A-19
Pentid-Sulfas for Syrup—Squibb A-126
Syndecon—Bristol A-128

Anticholinergics

Milpath—Wallace A-208
Pathibamate—Lederle A-152-153
Pro-Banthine with Dartal—Searle A-1

Anticoagulants

Athrombin-K—Purdue Frederick A-8
Coumadin—Endo A-58

Anticonvulsants

Dilantin—Parke-Davis A-15

Antidepressants

Catron—Lakeside A-108
Deprol—Wallace A-62-63
Nardil—Warner-Chilcott A-201
Niamid—Pfizer A-102
Tofranil—Geigy A-192

Antidiarrheals

Polymagma—Wyeth A-107
Sorboquel—White A-154-155-156-157

(Continued on page A-137)

A-2
A-179
A-133
A-160
A-191
A-70-71
A-29

A-132
A-145
A-84

A-91
A-12
9; A-49
-110-111

-170-171
-194-195

-37-38-39
-162-163
A-212
A-130
-182-183
-112-113
A-19
A-126
A-128

A-208
-152-153
A-1

A-8
A-58

A-15

A-108
A-62-63
A-201
A-102
A-192

A-107
55-156-157

NE

Schering

the first chlorinated steroid

dichlorisone acetate

newDILODERM™

specifically leveled at topical skin therapy

free from hazards of systemic absorption on topical application...**effective, economical**...for any steroid-responsive skin disorder...available as Foam Aerosol, Aerosol and Cream with or without neomycin

5-610

because.....

skin deep is deep enough

FREQUENTLY INDICATED FOLLOWING ACCIDENTS

PARAFLEX® FOR RELIEF OF PAINFUL MUSCLE SPASM

Chlorzoxazone*

When accidents result in sprains or strains, PARAFLEX reduces painful spasm promptly. Effective in a wide variety of rheumatic, arthritic and orthopedic disorders, PARAFLEX relieves pain, improves mobility and facilitates rehabilitation. Side effects seldom occur and are rarely severe enough to require discontinuation of therapy. □ *Average Dosage:* Two tablets t.i.d. or q.i.d. □ *Supplied:* Tablets, scored, orange, bottles of 50. Each tablet contains PARAFLEX, 250 mg.

McNEIL

*U.S. Patent No. 2,895,877

McNEIL LABORATORIES, INC · PHILADELPHIA 32, PA.

315A60

Products by Therapy Indications—*Continued*

Antiemetics
Tigan—Roche A-99

Anti-Inflammatories
Chymoral—Armour A-24
Kenalog in Orabase—Squibb A-128

Antipyretics
Tylenol—McNeil A-210

Antiseptics
Betadine—Tailby-Nason A-124

Antispasmodics
Bentyl—Merrell A-28

Ataractics
Librium—Roche A-166-167
Mellaril—Sandoz A-66-67
Meprospan—Wallace A-7
Miltown—Wallace ..... A-116; Facing A-116; A-164
Permitil—White A-21
Phenergan—Wyeth A-175
Timovan—Ayerst A-34-35-126
Vistaril—Pfizer A-148

Cardiovascular Agents
Digitaline Nativelle—Fougera A-134
Diupres—Merck Sharp & Dohme A-118-119
Elixophyllin—Sherman A-32
Equanil—Wyeth A-181
Equanitrate—Wyeth A-138
Hygroton—Geigy A-93
MER/29—Merrell ..... Facing A-132-133
Metamine—Leeming A-127
Miltrate—Wallace A-87
Moderil—Pfizer A-105
Oreticyl—Abbott A-186-187
Ostensin—Wyeth A-200
Pentritol—Armour A-197
Quinidine Sulfate—Davies, Rose A-211
Saluron—Bristol A-202-203
Serpasil—Ciba A-129
Serpasil-Apresoline—Ciba ..... Fourth Cover
Serpasil-Esidrix—Ciba A-51

Choleretics and Hydrocholeretics
Decholin—Ames A-33

Coagulants
Premarin Intravenous—Ayerst A-180

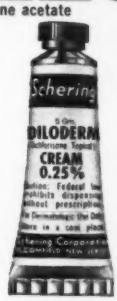
Contraceptives
Diaphragms—Ortho A-106
Ramses—Schmid A-60

Dermatologic Preparations
Altafur—Eaton A-79
Aristocort Acetonide—Lederle A-204
Cortisporin—Burroughs Wellcome A-161
Diloderm—Schering A-135-137-139-141
Neo-Aristocort Acetonide—Lederle A-204
Neo-Aristoderm—Lederle A-204-205

(Continued on page A-139)

Schering

new...
first chlorinated steroid
DILODERM™
dichlorisone acetate

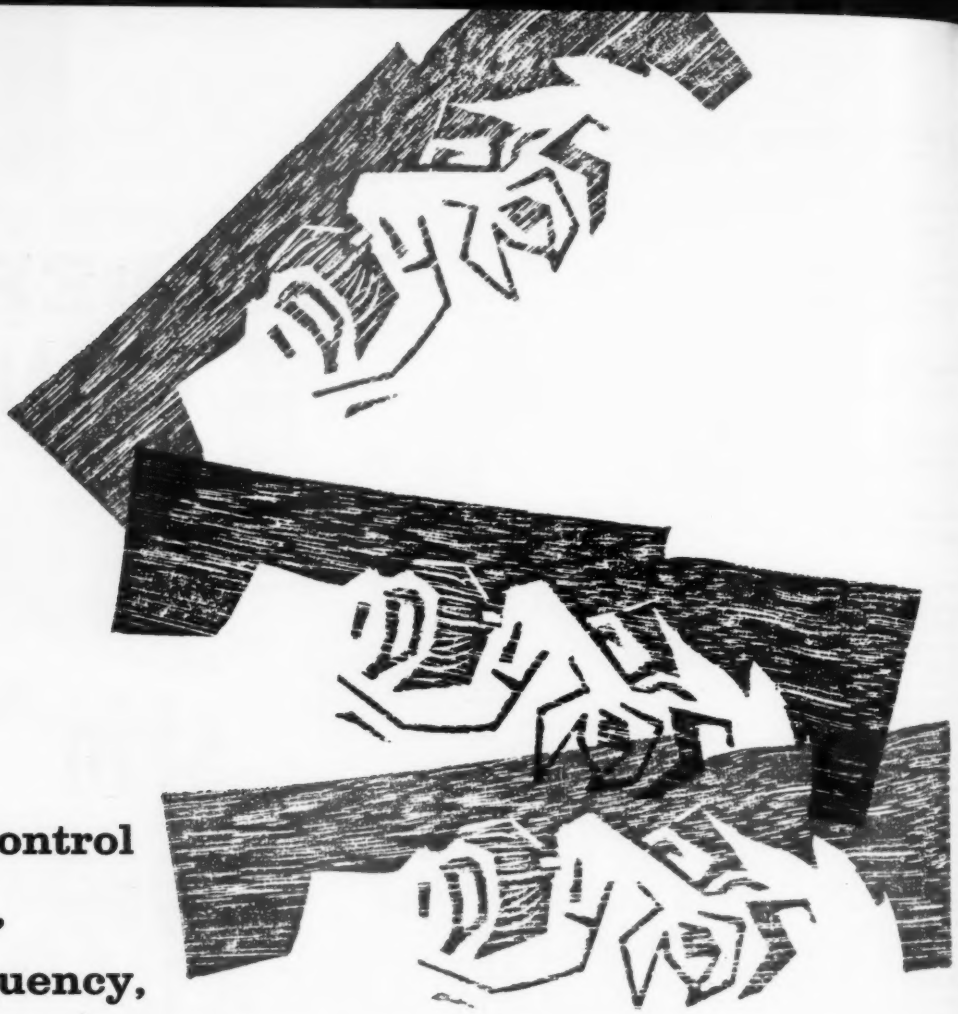


CREAM

specifically leveled at topical skin therapy...
as economical as hydrocortisone
...rapidly effective, buffered to maintain optimal skin pH.
DILODERM Cream 0.25% or NEO-DILODERM Cream (with 0.5% neomycin), 5 Gm. tubes.

because... skin deep is deep enough

S-619



To control fear, frequency, and severity of anginal attacks

Equanitrate*

Meprobamate and Pentaerythritol Tetranitrate, Wyeth

EQUANITRATE helps control pain and accompanying anxiety in angina pectoris. It reduces the number and severity of attacks, increases exercise tolerance, and lessens nitroglycerin dependence.

A recent double-blind study† comparing meprobamate, a placebo, PETN, and EQUANITRATE states: "The best results . . . in both clinical and electrocardiographic response, were observed with a combination of meprobamate and pentaerythritol tetranitrate [EQUANITRATE]. . . ."

For further information on prescribing and administering EQUANITRATE see descriptive literature, available on request.

Wyeth Laboratories Philadelphia 1, Pa.

†Russek, H.I.: Am. J. Cardiol. *3*:547 (April) 1959. *Trademark

Supplied: **EQUANITRATE 10** (200 mg. meprobamate, 10 mg. pentaerythritol tetranitrate), white oval tablets, vials of 50. **EQUANITRATE 20** (200 mg. meprobamate, 20 mg. pentaerythritol tetranitrate), yellow oval tablets, vials of 50.

100 ANNIVERSARY Wyeth

A Century of Service to Medicine

NeoDecadron—Merck Sharp & Dohme A-104
Neosporin—Burroughs Wellcome A-161
Ointment—Desitin A-13
Polysporin—Burroughs Wellcome A-161
Selsun—Abbott ..... Facing A-16
Triburon—Roche A-22-23
Triburon-HC—Roche A-22-23

Diagnostic Aids
TA-Test—Hyland A-100

Diuretics
Diuril—Merck Sharp & Dohme A-30-31
Esidrix—Ciba ..... Facing A-180-181

Fibrinolytics
Actase—Ortho A-199

Flatulence Therapy
Ilopan-Choline—Warren-Teed A-81

Gynecologic and Obstetric Medications
Bonine—Pfizer A-158-159
En-Cebrin—Lilly A-5
Filibon—Lederle A-95
Marplan—Roche A-140
Milprem—Wallace A-72
Natalins—Mead Johnson A-173
Norlutin—Parke-Davis A-103
Triburon—Roche A-198
Vasodilan—Mead Johnson A-131

Hematinics
Iberol—Abbott ..... Facing A-17

Laxatives, Enemas and Deconstipants
Enema—Fleet A-120
Instant Mix Metamucil—Searle A-128
Peri-Colace—Mead Johnson A-209
Senokot—Purdue Frederick A-9

Motion Sickness Therapy
Antivert—Roerig A-53

Musculoskeletal Disorders
Anturan—Geigy A-25
Butazolidin—Geigy A-177
Decadron—Merck Sharp & Dohme
..... Second Cover; A-206-207; Third Cover
Disipal—Riker A-61
Equagesic—Wyeth ..... Facing A-84-85; A-85
Hydeltra-T.B.A.—Merck Sharp & Dohme A-47
Pabalate—Robins A-121
Pabalate-HC—Robins A-121
Pabalate-Sodium Free—Robins A-121
Paraflex—McNeil A-136
Phenoxene—Pitman-Moore A-10
Rela—Schering A-168-169
Robaxin—Robins A-50
Robaxisal—Robins A-142-143
Sigmagen—Schering A-78
Soma—Wallace ..... Facing A-117; A-117
Triurate—McNeil A-124

(Continued on page A-141)

Schering

new...

first chlorinated steroid

DILODERM™

dichlorisone acetate

FOAM

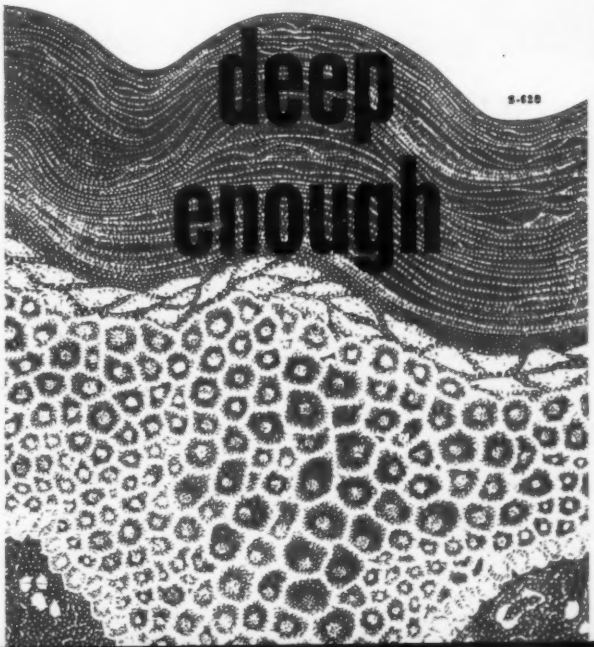
specifically leveled at topical skin therapy...

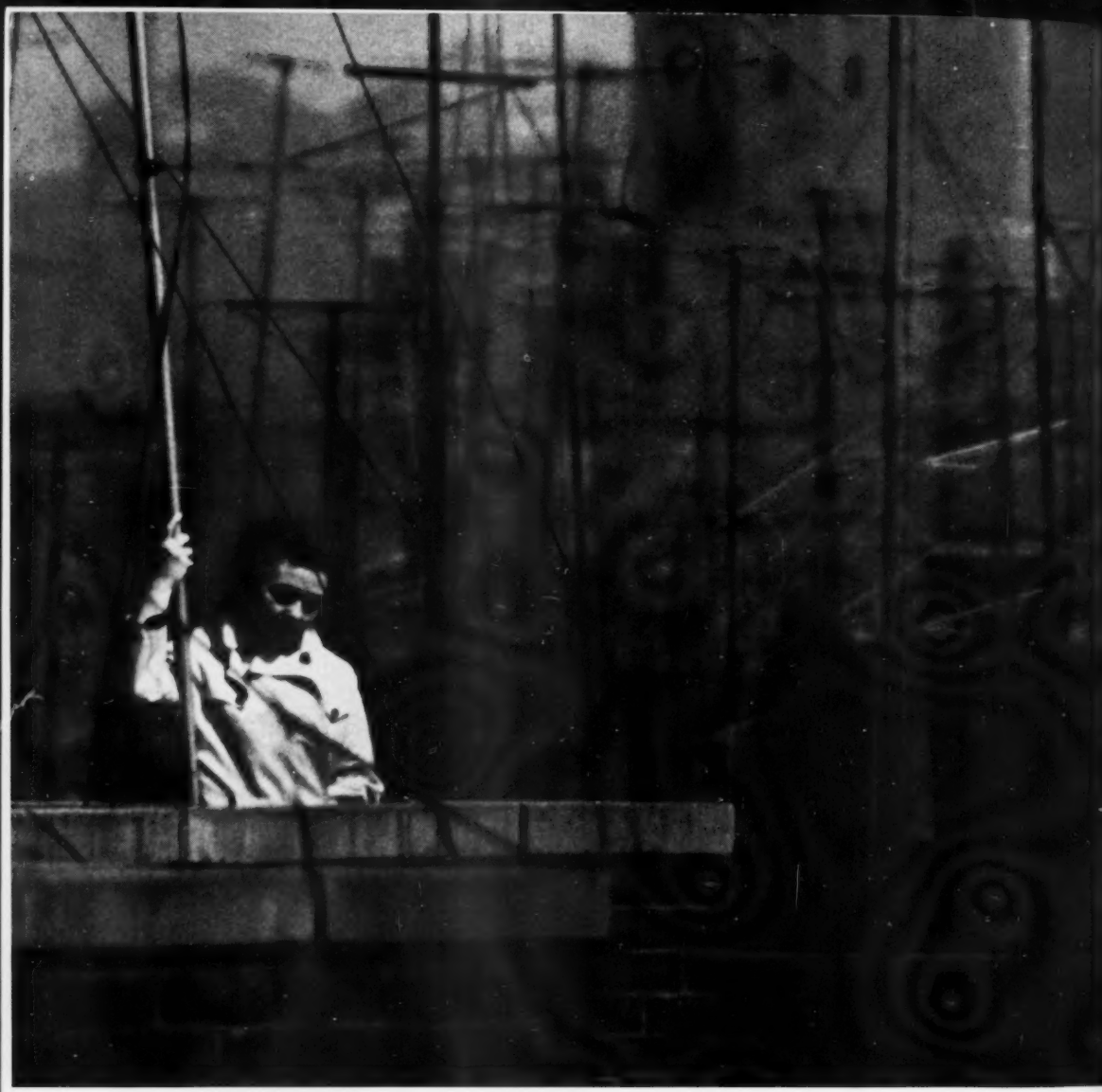
superior dispersibility; cosmetic elegance assures patient acceptance; economical in use... special valve prevents waste.

DILODERM Foam Aerosol or NEO-DILODERM Foam Aerosol (with neomycin), 10 Gm. container.

because...

skin deep is deep enough





When "change of life" seems the end of life..

With the advancing years, woman's vulnerability to depression often becomes intense. The future looms insecure; menopausal dysfunctions spark somatic concern. And as she faces losing a symbol of femininity, even suicidal panic may supervene.

Menopausal depression has been lifted by Marplan—even when withdrawal and loss of affect were severe.

Episodes of depression can often be controlled by a brief schedule of Marplan treatment, ordinarily 10 mg t.i.d. In some patients, release of new psychic energies may be seen on Marplan in as little as three or four days.

Extensive clinical trials have revealed no hepatitis attributable to Marplan. However, complete dosage information, available on request, should be consulted before administering Marplan.

Supplied: 10-mg tablets in bottles of 100 and 1000.

Marplan
a happy balance of potency/safety

MARPLAN®—1-benzyl-2-(5-methyl-3-isoxazolylcarbonyl)hydrazine

ROCHE
LABORATORIES
Division of Hoffmann-La Roche Inc.

Reducing Aids

Biphetamin—Strasenburgh A-101
Desoxyn Gradumet—Abbott A-122-123
Ionamin—Strasenburgh A-101
Metrecal—Mead Johnson A-150-151
Syndrox—McNeil A-16

Respiratory Medications

Benylin—Parke-Davis A-144
Caytine—Lakeside A-109
Naldecon—Bristol A-41

Sedatives and Hypnotics

Alurate—Roche A-55
Doriden—Ciba A-68-69
Noludar—Roche A-125

Urinary Anti-Infectives

Azo Gantrisin—Roche A-65
Mandelamine—Warner-Chilcott A-43
Palcillin—Phil. Ampoule A-128
Pyridium—Warner-Chilcott A-45

Vasopressors

Aramine—Merck Sharp & Dohme A-146-147

Vitamins and Nutrients

Beminal—Ayerst A-184
Dayalets—Abbott ..... Facing A-64-65
Durabolin—Organon A-57
Gevrabon—Lederle A-26-27
Gevral—Lederle A-26-27
Gevrine—Lederle A-26-27
Myadec—Parke-Davis A-89
Optilets—Abbott ..... Facing A-64-65
Rubramin PC—Squibb A-114-115
Sur-Bex with C—Abbott ..... Facing A-64-65
Vidaylin-M—Abbott A-130
Vi-Sol—Mead Johnson A-80

DIETARY

Carnalac—Carnation A-14
Citrus Fruits—Florida Citrus A-48
Evaporated Milk—Carnation A-14
Instant Milk—Carnation A-185
Pork—American Meat A-64

INSTRUMENTS AND EQUIPMENT

Accell—Victoreen Instrument A-126
Magnascaler—Picker A-130
Optiseal Serum Vial—Kimble Glass A-126
Pocket Cardiac Resuscitator—Medtronic A-130
Sharp-Et Hypodermic Needle—Randall Faichney A-128
Thermal Detector—Crescent Engineering A-124
Thermotic Drainage Pump—Gomco A-189
Visette—Sanborn A-149
Viso—Sanborn A-149
Viso-Cardiette—Sanborn A-149

MISCELLANEOUS

Disposable Eyecup—Busse Hosp. Products A-130
Disposable Litter Bag—Klean Kan Bag Co. A-130
Disposable Nipple Bag—Klean Kan Bag Co. A-128
Eye-Face Wash Fountain—Haws Drinking Faucet A-126
X-Ray and Photography Supplies—Eastman ..... Facing A-148-149

Schering

new...
first chlorinated steroid
DILODERM™
dichlorisone acetate

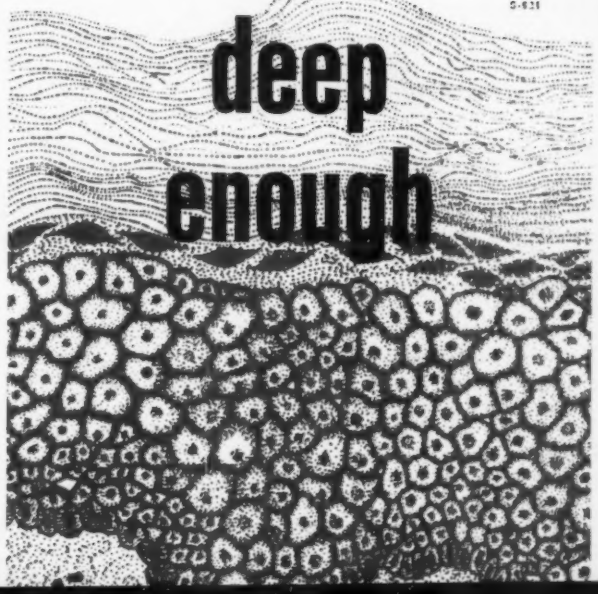
AEROSOL

specifically leveled at topical skin therapy...

rapid, prolonged relief in itching, burning dermatoses; especially for difficult-to-reach and hairy areas.

DILODERM Aerosol or NEO-DILODERM Aerosol (with neomycin) available in 50 Gm. containers.

because... skin deep is deep enough



now–for more comprehensive control of *'pain & spasm'*

INDICATIONS

HEAD: temporomandibular muscle spasm • NECK: acute torticollis, osteoarthritis of cervical spine with spasm of cervical muscles, whiplash injury • TRUNK AND CHEST: costochondritis, intercostal myositis, xiphodynia • BACK: acute and chronic lumbar strains and sprains, acute low back pain (unspecified), acute lumbar arthritis and traumatic injury, compression fracture, herniated intervertebral disc, post-disc syndrome, strained muscle(s) • EXTREMITIES: acute hip injury with muscle spasm, ankle sprain, arthritis (as of foot or knee), blow to shin followed by muscle spasm, bursitis, spasm or strain of muscle or muscle group, old fracture with recurrent spasm, Pellegrini-Stieda disease, tenosynovitis with associated pain and spasm.

-pain due to
or associated with
-spasm of skeletal muscle

a new muscle relaxant-analgesic

Robaxisal®

ROBAXIN® WITH ASPIRIN

Many conditions, painful in themselves, often give rise to spasm of skeletal muscles. ROBAXISAL, the new dual-acting muscle relaxant-analgesic, treats both the pain and the spasm with marked success: In clinical studies on 311 patients, 12 investigators[1] reported satisfactory results in 86.5%. Each ROBAXISAL Tablet contains:

- A relaxant component — Robaxin† — widely recognized for its prompt, long-lasting relief of painful skeletal muscle spasm, with unusual freedom from undesired side effects. . . . . 400 mg.

† Methocarbamol Robins. U.S. Pat. No. 2770645

- An analgesic component—aspirin—whose pain-relieving effect is markedly enhanced by Robaxin, and which has added value as an anti-inflammatory and anti-rheumatic agent. . . (5 gr.) 325 mg.

INDICATIONS: ROBAXISAL is indicated when analgesic as well as relaxant action is desired in the treatment of skeletal muscle spasm and severe concurrent pain. Typical conditions are disorders of the back, whiplash and other traumatic injuries, myositis, and pain and spasm associated with arthritis.

SUPPLY: ROBAXISAL Tablets (pink-and-white, laminated) in bottles of 100 and 500.

Also available: ROBAXIN Injectable, 1.0 Gm. in 10-cc. ampul. ROBAXIN Tablets, 0.5 Gm. (white, scored) in bottles of 50 and 500.

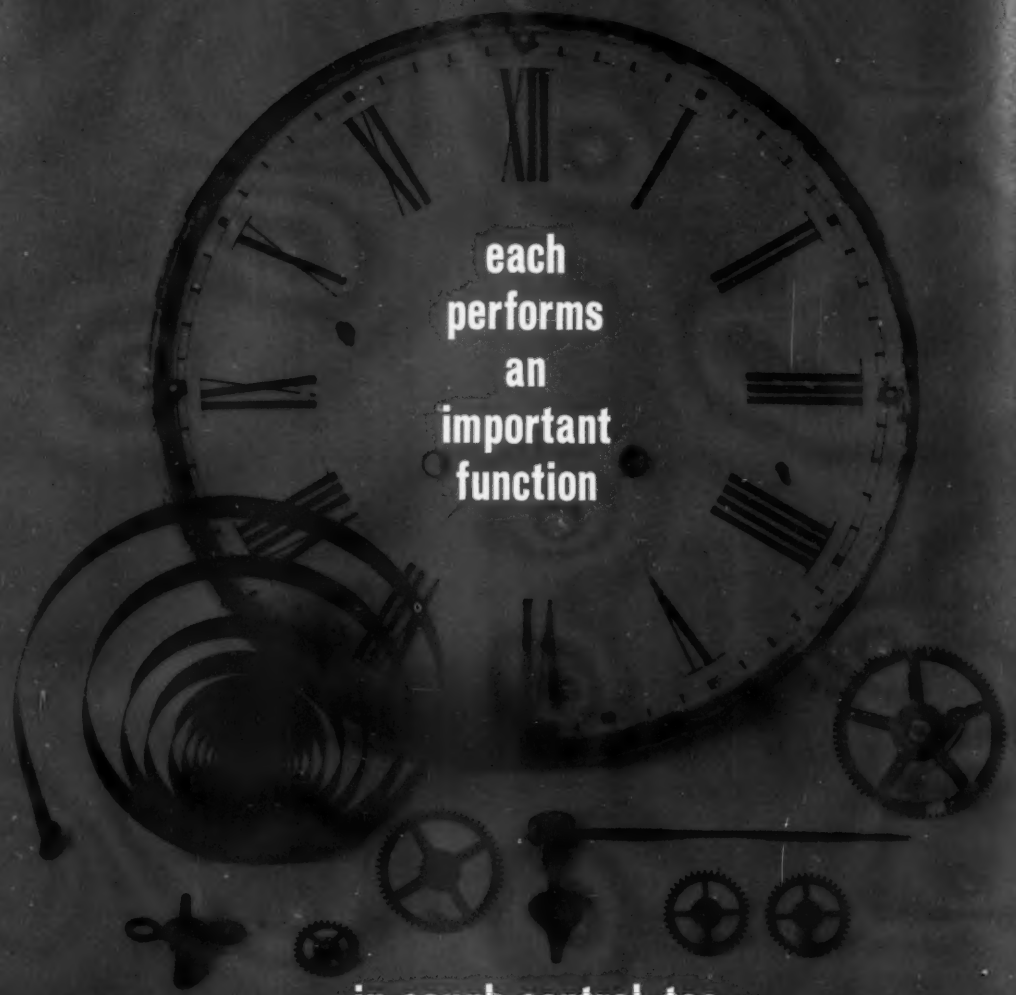
[1]Clinical reports in files of A. H. Robins Co., Inc., from: J. Allen, Madison, Wisc., B. Billow, New York, N. Y., B. Decker, Richmond, Va., C. Freeman, Jr., Augusta, Ga., R. B. Gordon, New York, N. Y., J. E. Holmblad, Schenectady, N. Y., L. Levy, New York, N. Y., N. LoBue, Chicago Heights, Ill., H. Nachman, Richmond, Va., A. Poindexter, Los Angeles, Cal., E. Rogers, Brooklyn, N. Y., K. H. Strong, Fairfield, Ia.

Additional information available upon request.

Robins

A. H. ROBINS CO., INC., Richmond 20, Virginia

Making today's medicines with integrity . . . seeking tomorrow's with persistence



in cough control, too—
each component contributes to the efficacy of

BENYLIN® EXPECTORANT

potent antihistaminic—relieves nasal stuffiness, sneezing, lacrimation, itching, and bronchial congestion

proven expectorants—liquefy and loosen tenacious mucus...help clear the respiratory tree

time-tested antispasmodic—decreases bronchospasm; helps quiet the cough reflex

palatable demulcent—raspberry-flavored syrup soothes raw, irritated throat membranes...pleasant taste is readily acceptable to patients of all ages

BENYLIN EXPECTORANT contains in each fluid-ounce:

Benadryl® hydrochloride (diphenhydramine hydrochloride, Parke-Davis)	80 mg.
Ammonium chloride	12 gr.
Sodium citrate	5 gr.
Chloroform	2 gr.
Menthol	0.1 gr.
Alcohol	5%

supplied: BENYLIN EXPECTORANT is available in 16-ounce and 1-gallon bottles. 27860

PARKE-DAVIS

PARKE, DAVIS & COMPANY • DETROIT 32, MICHIGAN

all quiet on the ulcer front Even under stress and tension Gelusil antacid adsorbent keeps peptic ulcer patients pain-free all day long. Gelusil is the only antacid that coats the ulcer with two protective, long-lasting, acid-adsorbing gels while simultaneously removing excess acid. Pleasant-tasting Gelusil is *all* antacid—nonconstipating—contains no laxative.

GELUSIL®

the physician's antacid

WARNER CHILCOTT

MORRIS PLAINS, N.J.

combat HYPOTENSION

raise and maintain blood pressure with knowledge that "distressing side effects, such as thrombophlebitis or tissue slough, do not occur."[1]

INJECTION

ARAMINE® BITARTRATE

(metaraminol bitartrate)

for vasopressor action with a choice of routes

ARAMINE has gained rapid acceptance as a practical vasopressor for combatting hypotension due to hemorrhage and surgical complications. Administer ARAMINE by subcutaneous or intramuscular injection, by intravenous infusion or by direct intravenous injection as the clinical situation demands. Extravascular deposition has not resulted in tissue slough, necrosis or thrombophlebitis.[1-4] Expect a smooth, sustained vasopressor effect with no secondary fall in blood pressure. There are no reports of tachyphylaxis or hyperglycemia.

ARAMINE is equally valuable in treatment of shock accompanying anaphylaxis, myocardial infarction, brain damage and infectious disease.

supplied: in 1-cc. ampuls and 10-cc. vials (10 mg. per cc.).

references: 1. Circulation 13:834, June 1956.
2. Am. J. M. Sc. 230:357, Oct. 1955.
3. Circulation 16:1096, Dec. 1957.
4. J.A.M.A. 163:1482, April 20, 1957.

ARAMINE is a trademark of Merck & Co., Inc.

MERCK SHARP & DOHME
Division of Merck & Co., Inc. Philadelphia 1, Pa.

When panic strikes your preoperative patient

VISTARIL, as part of a preoperative regimen, can safely relax your patients by allaying fear and apprehension. They are able to sleep soundly at night, and usually remain calm but alert during the day. Postoperatively, VISTARIL quiets anxiety and controls emesis.

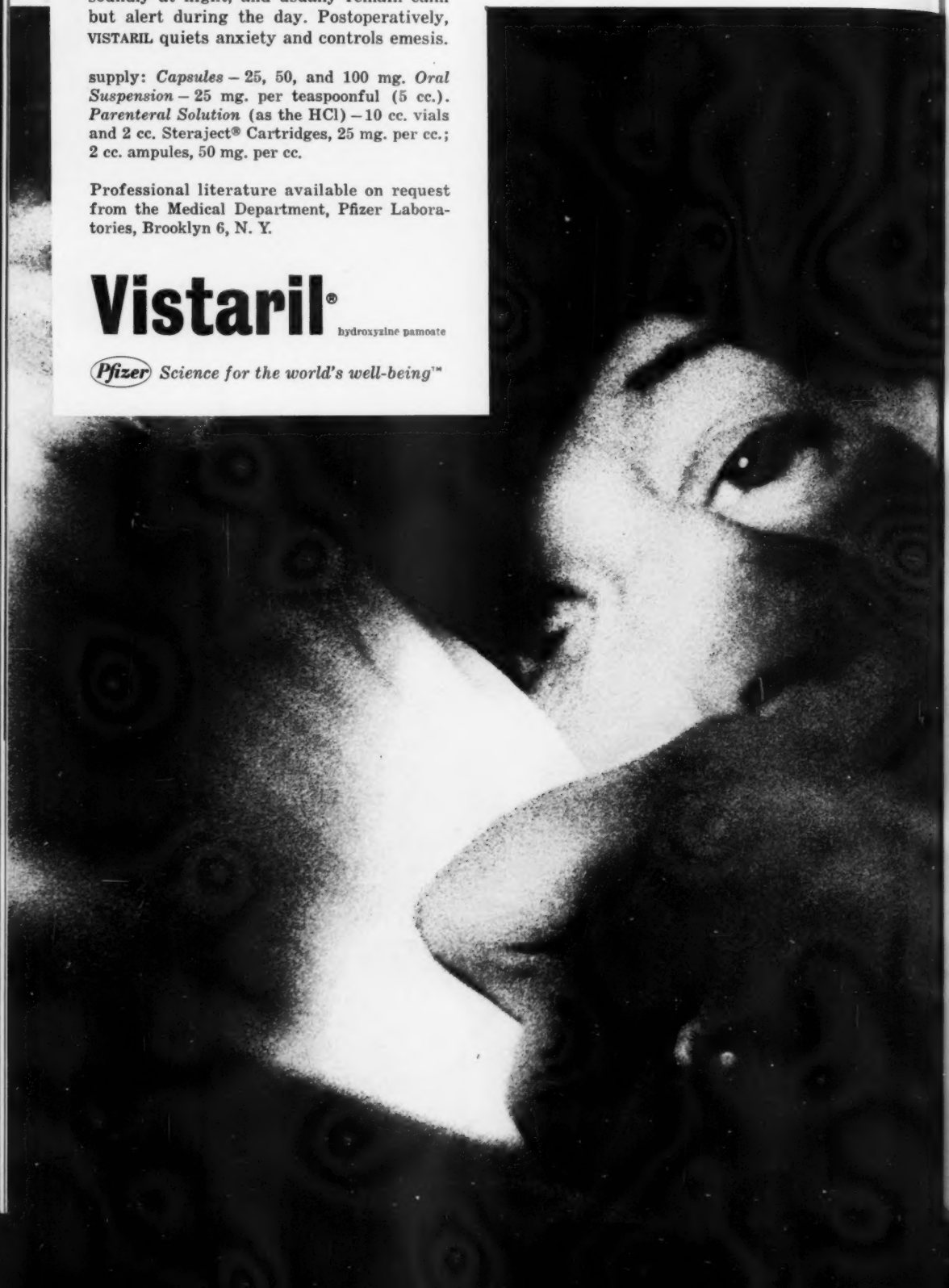
supply: *Capsules* – 25, 50, and 100 mg. *Oral Suspension* – 25 mg. per teaspoonful (5 cc.). *Parenteral Solution* (as the HCl) – 10 cc. vials and 2 cc. Steraject® Cartridges, 25 mg. per cc.; 2 cc. ampules, 50 mg. per cc.

Professional literature available on request from the Medical Department, Pfizer Laboratories, Brooklyn 6, N. Y.

Vistaril®

hydroxyzine pamoate

Pfizer *Science for the world's well-being™*



Splenoportogram (on Kodak Blue Brand Medical X-ray Film) of patient with cirrhosis of liver showing obstructed hepatic circulation and collateral veins including gastric and esophageal varices.

The technic of SPLENOPORTOGRAPHY:

5 steps recorded on Ektachrome Film

People, long ago, had words for it . . . "One picture is better than a thousand words." True then; truer than ever today, when words and color illustrations may be combined to outline the steps in any technic or procedure. Surely, every physician who has a story to tell—procedures to describe—should investigate color photography. The cost of equipment and processing is small, the rewards great.

1. Equipment for splenic manometrics: Saline manometer; cups with contrast material, procaine, skin antiseptics and saline; syringes; connecting plastic tubes; stopcocks; needles; forceps.

2. With patient in supine position on x-ray table, tube is centered over upper abdomen. Radiographs are made serially one per second during injection over a period of 15 seconds, after which they are obtained at 5-second intervals.

3. Thin-wall, 16-gauge needle inserted through ninth intercostal space in midaxillary line has entered spleen. Local anesthesia used.

4. Pliable plastic tube connects saline manometer to needle. Splenic pulp pressures, corrected to the level of right atrium, indicate portal pressures.

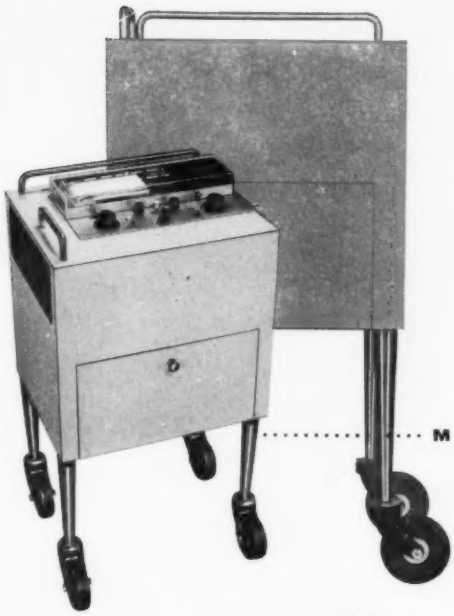
5. Contrast material is being injected rapidly into splenic pulp as radiographs are obtained. (Figure 2).

From Kodak come medical x-ray films— Kodak Blue Brand and Kodak Royal Blue (Royal Blue, Kodak's fastest x-ray film, is designed to assure minimum exposure for each examination). **Kodak color materials** are available for every photographic purpose: *For miniature and motion-picture cameras—* Kodachrome Film; *for sheet film cameras—* Kodak Ektachrome Film and Kodak Ektacolor Film; *for roll-film and miniature cameras—* Kodak Ektachrome Film and Kodacolor Film; also a variety of Kodak color print materials.

Order Kodak x-ray products from your Kodak x-ray dealer,
Kodak photographic products from your Kodak photographic dealer.

Kodak
TRADE MARK

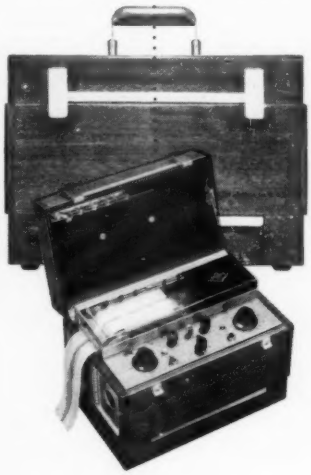
***Medical Division,* EASTMAN KODAK COMPANY, Rochester 4, N.Y.**



MOBILITY

PORTABILITY

OFFICE VERSATILITY



The case for your electrocardiograph

Why not just one "all-purpose" electrocardiograph — for house calls... office use with a choice of chart speeds, sensitivities, recording capabilities . . . mobile "heart station" use in clinics and hospitals? Because *each* need calls for *specific, individual* instrument characteristics — as found in these three Sanborn electrocardiographs.

The Sanborn Model 300 Visette weighs only 18 pounds, is as small as a brief case, has rugged, largely transistorized circuitry. *The Model 100 Viso-Cardiette* is also portable, but expressly designed for use where the versatility of *two* chart speeds, *three* sensitivities, and provision for *monitoring* and *other* types of recording are desired. The third Sanborn instrument is the *Model 100M "Mobile Viso"* — identical in circuitry to the 100, but in a mobile cabinet of either mahogany or rugged, stain-resistant plastic laminate.

Each ECG has *particular* usefulness . . . and each offers *proven* design and performance. Ask your nearby Sanborn man to demonstrate the instrument of your choice — designed for *your* needs.

SANBORN COMPANY

MEDICAL DIVISION, 175 Wyman St., Waltham 54, Massachusetts

measured calories for adequate nutrition with high satiety on 900 calories a day—without appetite depressants

METRECAL™

DIETARY FOR WEIGHT CONTROL

adequate nutrition in 900-calorie program

One-half pound of Metrecal powder, the daily 900-calorie feeding, provides 70 grams of high-grade protein plus vitamins and minerals to meet or exceed all established minimum daily requirements. Metrecal itself *is* the diet—the *complete* diet.

impressive clinical results

in uncomplicated overweight: In a twelve-day study of 100 patients[1] on the Metrecal 900-calorie program, the average total weight loss per subject was 6½ pounds (over ½ pound a day). In another study,[2] patients on the 900-calorie Metrecal program for two to thirty weeks showed a weight loss per patient of 3 to 5 pounds weekly during the initial weeks and 2 to 2½ pounds per patient per week thereafter.

in overweight complicated by illness: In a study of 42 overweight patients,[3] some with serious medical disorders such as arthritis, cardiovascular disease, diabetes mellitus and gout, the 900-calorie daily Metrecal program provided an average total weight loss of 6.3 pounds per patient during the first week. The investigator encountered no significant complications in the management of these patients.

excellent patient cooperation

All investigators[1,2,3] commented on excellent patient cooperation. This was attributed to the effective loss of weight, the satiety of Metrecal which satisfied hunger in a majority of patients, its simplicity of use—no calorie counting or menu planning required—and its palatability. No appetite depressants were required.

flexibility in use

When more than 900 calories are permitted, either the daily allotment of ½ pound of Metrecal may be increased or it may be used in conjunction with low-calorie foods. Metrecal may also be used for one or two meals a day or as the total diet two or three days a week.

easy to use

All patients do to make a full day's supply of Metrecal beverage is mix ½ pound of Metrecal powder with a quart of water. Or they may make a glassful at a time. For variety, Metrecal is available in Plain, Chocolate or Butterscotch flavors.

Weight-Control Guide for patient instruction is available from your Mead Johnson representative, or by writing to us, Evansville 21, Indiana.

references. (1) Antos, R. J.: Southwestern Med. *40*:695-697 (Nov.) 1959. (2) Tullis, I. E.: Initial Experience with a Simple Weight Control Formula, to be published. (3) Roberts, H. J.: Effective Long-Term Weight-Reduction—A Therapeutic Breakthrough, to be published.

Mead Johnson

Symbol of service in medicine

99180

control the tension—treat the trauma

...Pathibamate® 400 200

meprobamate with PATHILON® tridihexethyl chloride Lederle

greater flexibility in the control of tension, hypermotility and excessive secretion in gastrointestinal dysfunctions

PATHIBAMATE combines two highly effective and well-tolerated therapeutic agents:

meprobamate (400 mg. or 200 mg.) widely accepted tranquilizer and . . .

PATHILON (25 mg.)—anticholinergic noted for its peripheral, atropine-like action, with few side effects.

The clinical advantages of PATHIBAMATE have been confirmed by nearly two years' experience in the treatment of duodenal ulcer; gastric ulcer; intestinal colic; spastic and irritable colon; ileitis; esophageal spasm; anxiety neurosis with gastrointestinal symptoms and gastric hypermotility.

Two dosage strengths—PATHIBAMATE-400 and PATHIBAMATE-200 facilitate individualization of treatment in respect to both the degree of tension and associated G. I. sequelae, as well as the response of different patients to the component drugs.

Supplied: **PATHIBAMATE-400**—Each tablet (yellow, ½-scored) contains meprobamate, 400 mg.; PATHILON tridihexethyl chloride, 25 mg.
PATHIBAMATE-200—Each tablet (yellow, coated) contains meprobamate, 200 mg.; PATHILON tridihexethyl chloride, 25 mg.

Administration and Dosage: **PATHIBAMATE-400**—1 tablet three times a day at mealtime and 2 tablets at bedtime.
PATHIBAMATE-200—1 or 2 tablets three times a day at mealtime and 2 tablets at bedtime.
Adjust to patient response.

Contraindications: glaucoma; pyloric obstruction, and obstruction of the urinary bladder neck.

Lederle LEDERLE LABORATORIES, A Division of AMERICAN CYANAMID COMPANY, Pearl River, New York

NOW... the first truly effective and safe control of both **chronic** and acute **diarrhea**

Sorboquel T.M.

(polycarbophil - thihexinol methylbromide)

IN CONVENIENT TABLET FORM

A totally new agent, for non-opiate control of the dual problem of diarrhea: too fluid feces, too frequent evacuations

Unexcelled therapeutic response, 85% of the chronic cases, 93% of the acute.[1-3]

The culmination of a decade of laboratory experimentation and over five years of clinical confirmation.

For too fluid feces, an extraordinary ability to absorb free fecal water.

For too frequent evacuations, superior, yet selective, antimotility action.

Convenient tablet form; simple, uncomplicated dosage schedule (1 tablet q.i.d.).

Even where all other agents have failed— Sorboquel arrests long-standing, uncontrolled, exhausting diarrheas

Unexcelled Therapeutic Response: Results of the Administration of Sorboquel Tablets[1-3]

	No. of Patients	*Response*		
		Excellent	*Good*	*Poor*
Chronic Diarrhea*	**485**	335	76	74
		84.7%		15.3%
Acute Diarrhea**	**332**	288	22	22
		93.4%		6.6%

*Chronic diarrheas include irritable bowel syndrome, regional enteritis, diverticulitis and ulcerative colitis, postantibiotic enteritis, malabsorption syndrome, radiation proctitis, surgically short-circuited intestinal states. Diarrhea had persisted for more than a year in a large percentage with bowel movement frequency averaging from 5 to more than 10 a day. In most patients, SORBOQUEL controlled the condition within 3 days, even where other agents had failed.

**Acute diarrheas include nonspecific gastroenteritis, enteritis, enterocolitis. Control of the diarrhea was achieved within 24 hours in most cases.

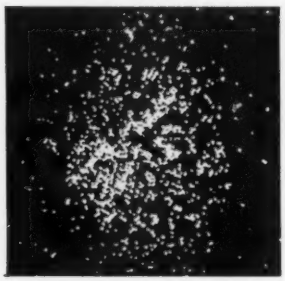
Dual-action **Sorboquel** arrests diarrhea even where all other agents have failed

The components in Sorboquel: the culmination of many years of development

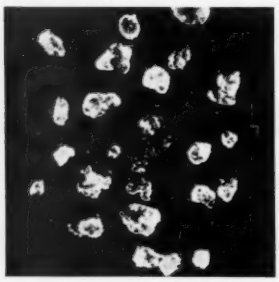
SORBOQUEL Tablets combine two unique and hitherto unavailable antidiarrheal agents—polycarbophil and thihexinol methylbromide. Acting together, through different but complementary mechanisms, these components in SORBOQUEL *absorb* free fecal water and *quell* hypermotility and associated spasm to an exceptional degree.

For too fluid feces, an extraordinary ability to absorb free fecal water

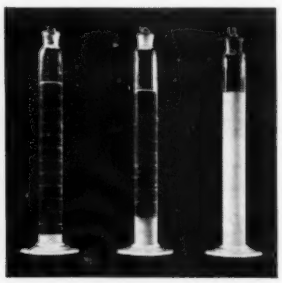
(through the hydrosorptive action of new polycarbophil)



Dry State
Demonstration of the particulate nature of dry polycarbophil.



Swollen State
Note the particulate nature of swollen polycarbophil. Impaction is virtually impossible.



(a) (b) (c)

Demonstration of the dependence of swelling of polycarbophil on pH (a) pH of stomach; (b) pH of duodenum; (c) pH of intestines.

A newly synthesized macromolecular substance exhibiting extraordinary capacity for absorption and retention of free fecal water[9-11] ■ the colloidal suspension is free-flowing, since, in the swollen or hydrated state, the particulate structure is retained[9] ■ exerts marked hydrosorptive action only on reaching the alkaline medium of the small intestine and colon ■ virtually free of impaction qualities ■ pharmacologically inert, not absorbed from the gut[12]

Convenient tablet form; simple, uncomplicated dosage schedule

SORBOQUEL DOSAGE: For older children and adults, initial dosage of one SORBOQUEL Tablet q.i.d. is usually adequate. Severe diarrheas may require six, or even eight, tablets in divided daily doses. (Dosages exceeding six tablets a day should not be employed over prolonged periods.) Many patients can be maintained on one to three tablets daily after the diarrhea is brought under control.

SIDE EFFECTS: The incidence of side effects at recommended dosage is negligible. (The usual precautions when using parasympatholytic agents should be observed. *Complete information regarding the use of* SORBOQUEL TABLETS *is available on request.*

DUAL ACTION

Sorboquel

TABLETS

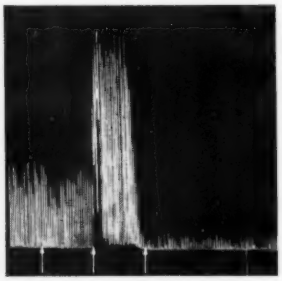
the first truly effective agent to control the dual problem of diarrhea: too fluid feces, too frequent evacuations

For too frequent evacuations, superior, yet selective, antimotility action

(through the parasympatholytic action of thihexinol methylbromide)

90-minute film demonstrating hypermotility of gastrointestinal tract in patient.

6-hour film after administration of thihexinol to patient showing marked inhibition of gastrointestinal motility.



(a) (b) (c)

Inhibition of methacholine-induced spasm by thihexinol in isolated rabbit intestine. Time of graph is 40 minutes. (a) normal motility; (b) methacholine, 40 mcg./L; (c) thihexinol, 10 mcg./ml.

A new, superior parasympatholytic agent with a dominant inhibitory action on intestinal motor function[13-16] ■ onset of intestinal motor inhibition has been shown to occur within *10-20 minutes*[14] ■ does not interfere with gastric secretion or digestive processes ■ unusually free from atropine-like side effects ■ its enteral antimotility action permits polycarbophil to exert maximal water-binding effect

SUPPLIED: SORBOQUEL TABLETS, bottles of 50 and 250. Each tablet contains 0.5 Gm. polycarbophil and 15 mg. thihexinol methylbromide.

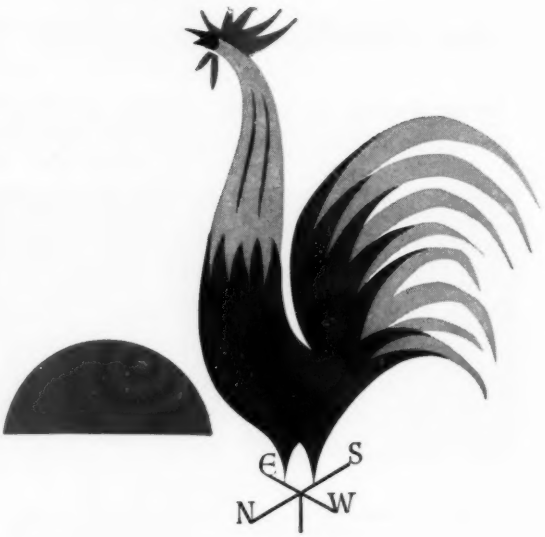
REFERENCES: 1. Hock, C. W.: Med. Times **88**:320 (March) 1960. 2. Winkelstein, A.: Personal communication. 3. Berkowitz, D.: in press. 4. Lind, H. E.: Personal communication. 5. Seneca, H.: in press. 6. Riese, J. A.: Personal communication. 7. Gilbert, A. S.; Schwartz, I. R., and Matzner, M. J.: Submitted for publication. 8. Personal communications to Medical Department, White Laboratories, Inc. 9. Pimparker, B. D.; Paustian, F. F.; Roth, J. L. A., and Bockus, H. L.: To be published. 10. Texter, E. C.: Personal communication. 11. Clinical reports to Medical Department, White Laboratories, Inc. 12. Grossman, A. J.; Batterman, R. C., and Leifer, P.: J. Am. Geriat. Soc. **5**:187 (Feb.) 1957. 13. McHardy, G.; Browne, D.; McHardy, R.; Bodet, C., and Ward, S.: Am. J. Gastroenterol. **24**:601 (Dec.) 1955. 14. Shay, H.: Personal communication. 15. Hirsh, H.: Personal communication. 16. Bercovitz, L. T.: J. Am. Geriat. Soc. **5**:940 (Nov.) 1957.

WHITE LABORATORIES, INC., *Kenilworth, New Jersey*

for morning sickness

brand of meclizine hydrochloride *

Bonine



DOSAGE:
One or two tablets give 24 hour protection. Administer at bedtime to prevent "next morning" sickness.

*Trademark

basic by every standard

effectiveness ✓

"Also, there are fewer therapeutic failures when patients are treated with . . . [BONINE] than with the other drugs."[1] "... [BONINE] is highly effective in relieving the nausea and vomiting of pregnancy, providing also the advantage of prolonged action. Thus, patients need not anticipate medication in the early morning hours when nausea is at its worst."[2]

safety ✓

"... [BONINE] is a drug which is safe and nontoxic to both the mother and fetus and which is attended by a minimum of undesirable side effects."[3]

toleration ✓

"The incidence of side effects is very low and this agent exhibits less sedation and somnolence within therapeutic ranges than any of the effective antiemetic agents."[1]

"Side effects were conspicuous by their rarity."[2]

convenience ✓

"The most striking advantage of... [BONINE] was that the administration of an effective dose only once daily, at bedtime, gave 24 hour protection, thus obviating the inconvenience and distress of repeating doses during the day."[4] "... [BONINE] is especially effective and has the advantages of a long duration of action (up to 24 hours) and a minimum of untoward side reactions."[1]

economy ✓

A single low-dosage drug providing therapeutic benefit at reasonable cost... contains no unnecessary added ingredients that increase cost... requires no extended-action tablet structure for prolonged effect.

experience ✓

The value of BONINE as an antinauseant has been well documented and is supported by six years of successful clinical use.[1-16]

only rarely does one drug meet so well the needs of one condition

REFERENCES: 1. Moyer, J. H.: M. Clin. North America, Mar., 1957, p. 405. 2. Lebherz, T. B., and Harris, J. H.: Obst. & Gynec. 6:606, 1955. 3. Mulherin, C. McL., and Bryans, C. I., Jr.: J. M. A. Georgia 45:46, 1956. 4. Bass, R. F.: Mississippi Doctor 32:176, 1954. 5. Seidner, H. M.: Illinois M. J. 109:20, 1956. 6. Charles, C. M.: Geriatrics 11:110, 1956. 7. Weil, L. L.: J. Florida Acad. Gen. Practice 4:9, No. 3, 1954. 8. Kinney, J. J.: J. M. Soc. New Jersey 53:128, 1956. 9. Semmens, J. P.: Obst. & Gynec. 9:586, 1957. 10. Conner, P. K., Jr., and Moyer, J. H.: GP 14:124, No. 5, 1956. 11. Daeschner, C. W., et al.: South. M. J. 49:1465, 1956. 12. Report of study by Army, Navy, Air Force Motion Sickness Team: J.A.M.A. 160:755, 1956. 13. Kean, B. H.: GP 20:112, No. 6, 1959. 14. Seppänen, A.: Geriatrics 14:457, 1959. 15. Hardman, E. F.: North Carolina M. J. 20:298, 1959. 16. Master, A. M.: New York J. Med. 58:2712, 1958.

SUPPLIED
BONINE Tablets, scored, 25 mg.
BONINE Chewing Tablets, mint-flavored, 25 mg.
BONINE Elixir, cherry-flavored, equiv. 12.5 mg./5 cc.

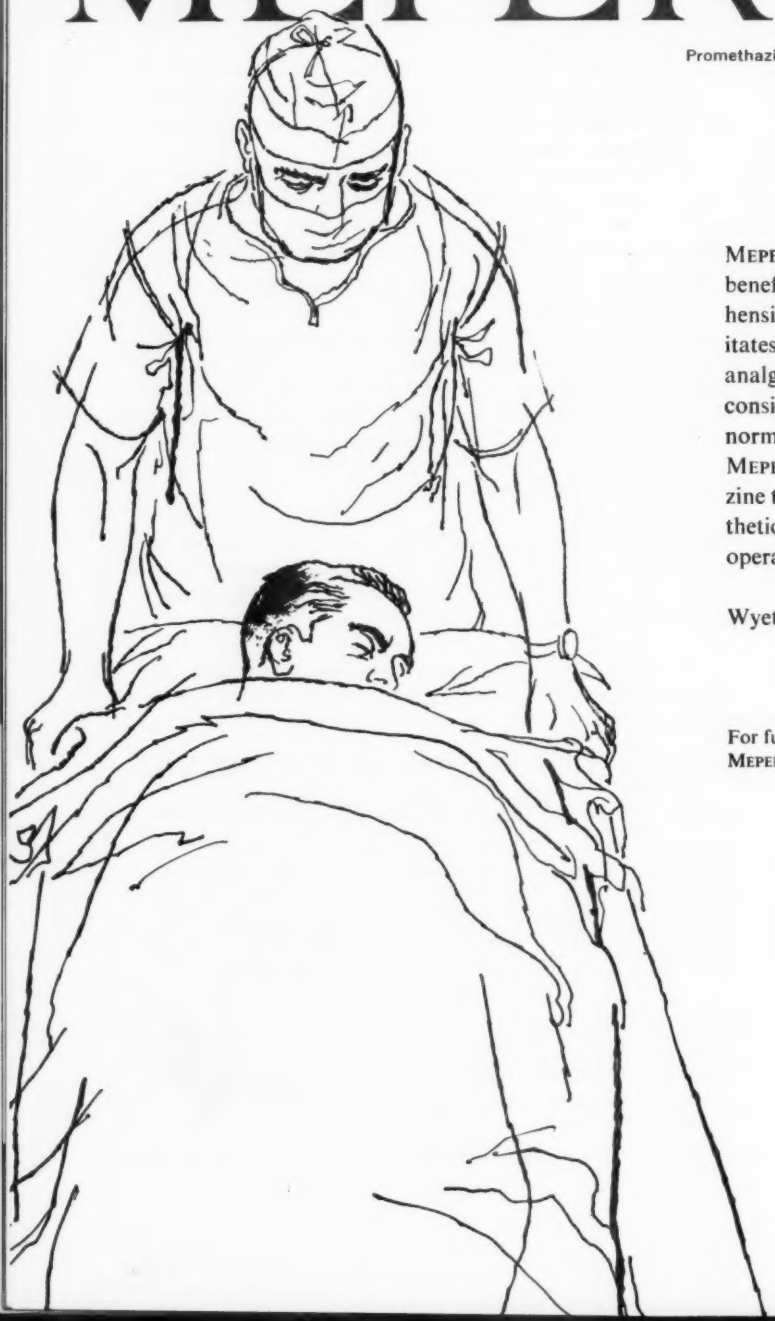
Professional Information Available on Request

PFIZER LABORATORIES Division, Chas. Pfizer & Co., Inc. Brooklyn 6, N. Y. Pfizer *Science for the world's well-being™*

for enhanced surgical analgesia—*meperidine-promethazine combine*

MEPERGAN

Promethazine Hydrochloride and Meperidine Hydrochloride, w



MEPERGAN provides both analgesic and seda benefits for the surgical patient. It allays ap hension, controls nausea and vomiting, and f itates anesthesia. Preoperative and postopera analgesia and sedation may be attained wi considerably smaller dose of the narcotic tha normally used. For inclusive perisurgical MEPERGAN—with its proved 1:1 ratio of promet zine to meperidine—provides premedication, a thetic action during surgery, and control of p operative pain.

Wyeth Laboratories Philadelphia 1, Pa.

For further information on prescribing and administeri MEPERGAN see descriptive literature, available on reque

100 ANNIVERSARY Wyeth ®

A Century of Service to Medicine

For topical infections, choose a 'B. W. & Co.'® 'SPORIN'...

'CORTISPORIN'®
brand OINTMENT
Combines the anti-inflammatory effect of hydrocortisone with the comprehensive bactericidal action of the antibiotics.

Each gram contains:
'Aerosporin'® brand Polymyxin B Sulfate 5,000 Units
Zinc Bacitracin ..... 400 Units
Neomycin Sulfate ..... 5 mg.
Hydrocortisone ..... (1%) 10 mg.
in a special petrolatum base.

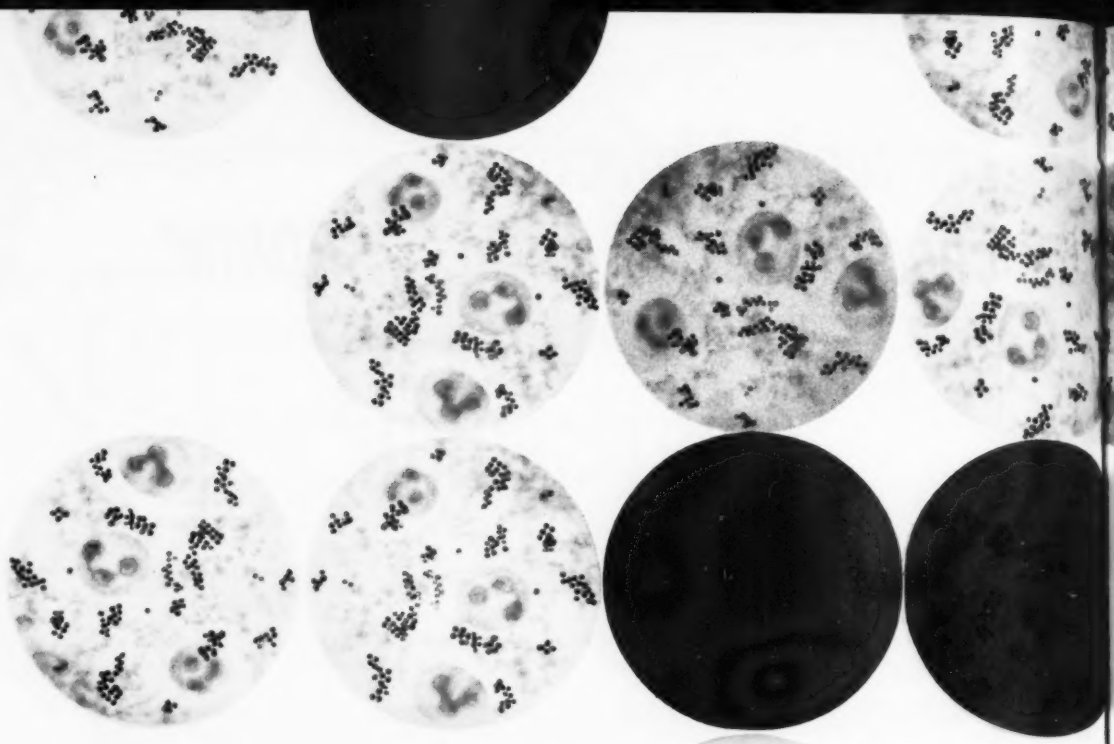
Provides comprehensive bactericidal action effective against virtually all bacteria likely to be found topically.
'NEOSPORIN'®
brand ANTIBIOTIC OINTMENT

Each gram contains:
'Aerosporin'® brand Polymyxin B Sulfate 5,000 Units
Neomycin Sulfate ..... 5 mg.
Zinc Bacitracin ..... 400 Units
in a special petrolatum base.

'POLYSPORIN'®
brand ANTIBIOTIC OINTMENT
Offers combined antibiotic action for treating conditions due to susceptible organisms amenable to local medication.

Each gram contains:
'Aerosporin'® brand
Polymyxin B Sulfate ..... 10,000 Units
Zinc Bacitracin ..... 500 Units
in a special petrolatum base.

BURROUGHS WELLCOME & CO. (U.S.A.) INC., Tuckahoe, N. Y.



repeatedly, clinicians report... effective results against staphylococci

"Chloramphenicol (CHLOROMYCETIN) was the only widely used antibiotic to which few of the strains were resistant."[1]

"Emergence of staphylococci resistant to chloramphenicol has rarely occurred since the development of this drug, except in an occasional clinic where it has had wide use in a closed population."[2]

"Chloramphenicol (CHLOROMYCETIN) has been an effective agent in the treatment of staphylococcal infections."[3]

"The antibiotic of choice in this series was chloramphenicol."[4]

CHLOROMYCETIN (chloramphenicol, Parke-Davis) is available in various forms, including Kapseals® of 250 mg. in bottles of 16 and 100.

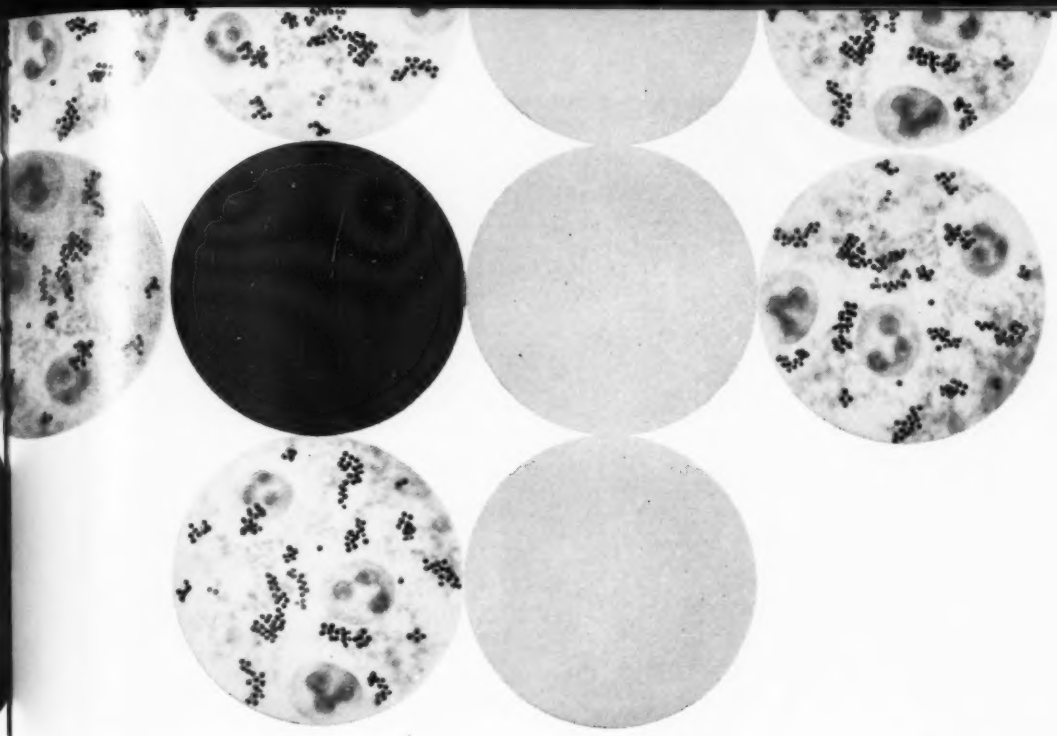
CHLOROMYCETIN is a potent therapeautic agent and, because certain blood dyscrasias have been associated with its administration, it should not be used indiscriminately or for minor infections. Furthermore, as with certain other drugs, adequate blood studies should be made when the patient requires prolonged or intermittent therapy.

References: (1) Finland, M.; Jones, W. F., Jr., & Bennett, I. L., Jr.: *Arch. Int. Med.* **104**:365, 1959. (2) Welch, H., in Welch, H., & Finland, M.: Antibiotic Therapy for Staphylococcal Diseases, New York, Medical Encyclopedia, Inc., 1959, p. 16. (3) Nichols, D. R., & Martin, W. J.: *Surg. Gynec. & Obst.* **107**:523, 1958. (4) Knight, I. C. S., & Nolan, B.: *Brit. M. J.* **1**:1224, 1959.

PARKE, DAVIS & COMPANY · DETROIT 32, MICHIGAN

33760

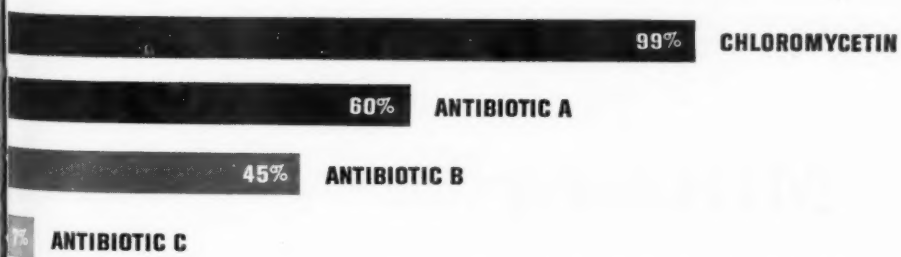
PARKE-DAVIS



CHLOROMYCETIN®

(chloramphenicol, Parke-Davis)

IN VITRO SENSITIVITY OF STAPHYLOCOCCUS AUREUS TO CHLOROMYCETIN AND TO THREE OTHER ANTIBIOTICS*



Staphylococcus aureus, coagulase-positive, was isolated in pure culture from 99 of 100 consecutive cases of puerperal breast abscess requiring surgical treatment.

Adapted from Knight & Nolan[1]

Miltown dispels your patient's fears and frustrations—the anxiety behind the tension.

Relieves the anxiety behind the tension

Miltown not only calms the surface agitation of your nervous patient. It also helps you dispel the underlying fears and frustrations—the anxiety behind the tension.

And Miltown has none of the additional actions that you often find in many other tranquilizers. There are no antihistaminic, antiemetic, anticholinergic or adrenolytic effects. Furthermore, Miltown has a simple dosage schedule and does not produce cumulative effects, change in appetite or libido, ataxia, Parkinson-like symptoms, jaundice or agranulocytosis.

Miltown®
meprobamate (Wallace)

Usual dosage: One or two 400 mg. tablets t.i.d.
Supplied: 400 mg. scored tablets, 200 mg. sugar-coated tablets; or as MEPROTABS* – 400 mg. *unmarked*, coated tablets.

WALLACE LABORATORIES / *New Brunswick, N. J.*

CM-2060

*TRADE-MARK

Because he has something you haven't...

People today—because of advances in medicine and the increasing acceptance of the annual physical examination—are living longer.

As a result, industry is making available to workers increased insurance and old-age benefits. Business, for its executives and employees, offers pension plans, profit-sharing, stock options.

What is being done—or *can* be done—for *you?*

Mutual Benefit Life has considered the problem of accrual which you, as an *unincorporated individual,* face.

Whether you are starting in your profession or are already well-advanced in it, a Mutual Benefit Life agent—trained in his calling—can help you plan a long-range or short-range program for True Security now and for whenever you plan to retire.

May we have a Mutual Benefit Life man call on you—when you are least busy? We believe his specialized knowledge can prove helpful and welcome.

you need the protection of TRUE SECURITY—financial planning for you and your family by

MUTUAL BENEFIT LIFE

The Insurance Company for TRUE SECURITY

CLIP AND MAIL TODAY

The Mutual Benefit Life Insurance Company
Agency Dept. 65
Newark 1, New Jersey

Please send me a free copy of a handbook on the medical profession's financial problems—and their solution, to help me keep more of my earnings. This request does not obligate me in any way.

NAME_____

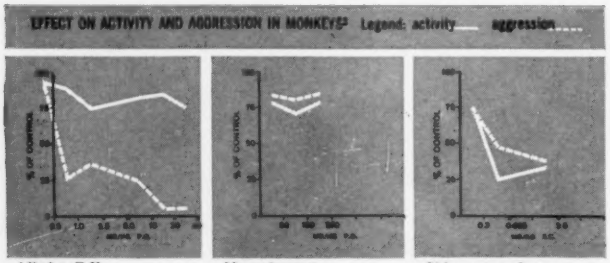
ADDRESS_____

CITY_____ ZONE____ STATE_____

Macaque monkey is characteristically vicious prior to Librium therapy.

Calm but alert, Librium-treated monkey offers striking contrast to "doped-up" appearance resulting from administration of reserpine and phenothiazine derivatives.

Calming and taming effect of Librium on rats, monkeys and mice



LibriumT.M.
Aggression dramatically reduced; **level of activity normal**

Meprobamate
No decrease in aggression; slight reduction of activity

Chlorpromazine
Aggression reduced; **precipitous decrease in activity**

Mice fight each other furiously under mild electric shock administered through bottom of cage. Librium-treated animals fail to show hostility.

Rage reaction (left) is elicited by lifting tail of rat made vicious by destruction of septal area in brain.

Septal rat (right) allows lifting by the tail after treatment with Librium. Rat remains alert.

the short ti e since its introduction, Librium has met with overwhelming acclaim om all parts the medical profession. Internists, psychiatrists, cardiologists, gyne- logists, der tologists and many other specialists, as well as tens of thousands of eneral pract oners, are discovering that the therapeutic applicability of this re- arkable new ompound transcends that of any tranquilizer or group of tranquilizers.

ere are pres nted some pertinent pharmacologic and clinical data documenting

mg—
d now
mg

EW LIBRIUM

the successor to the tranquilizers

uccessor in scope Librium covers the entire meprobamate range of erapy[8,9] plus a significant portion of the phenothiazine area[9] plus the difficult ddle ground between the two.[8] Librium is effective in obsessive-compulsive neuro- which previously have defied drug treatment.[3,4,7,8,17] Librium has a profoundly neficial effect on depression,[3,6,11] particularly the agitated type.[1,7,9]

uccessor in safety Librium is safer than the most widely prescribed nquilizing and "equanimity-producing" agents.[6,9,17] Librium lacks the autonomic cking effects of chlorpromazine and reserpine.[17] Librium is devoid of phenothia- e toxicity;[8,17] free of extrapyramidal complications;[17] and not encumbered by the pressions that often follow reserpine.[8]

ccessor in effect Librium, in addition to relieving anxiety, produces a ling of well-being, increased drive and a broadening of interest. Librium appears biggest step yet toward "a pure neuroleptic or 'easing' action totally distinct m a central sedative or hypnotic one."[16]

ES OF LIBRIUM: in the office patient troubled by anxiety and tension, and by the tability, fatigue and nervous insomnia associated with tension states

e office patient where you suspect anxiety and tension as contributing or causa- factors of organic or functional disorders

ore severely disturbed patients, including cases of agitated and reactive depres- fears, phobias, obsessions and compulsions

available:
IUM 5 mg, particularly useful in children, in geriatric patients, in the presence habilitating disease or wherever the situation may require more flexible dosage.

ied: Capsules, 10 mg, green and black; 5 mg, green and yellow—bottles of 50 and 500.
complete information on indications and recommended dosage, consult product literature.

Published Reports on Librium: 1. T. H. Harris, **Dis. Nerv. System, 21**:(Suppl.), 3, 1960. **2.** L. O. Randall, **ibid.**, p. 7. **3.** J. M. Tobin, I. F. Bird and D. E. Boyle, **ibid.**, p. 11. **4.** H. A. Bowes, **ibid.**, p. 20. **5.** J. Kinross-Wright, I. M. Cohen and J. A. Knight, **ibid.**, p. 23. **6.** H. H. Farb, **ibid.**, p. 27. **7.** C. Breitner, **ibid.**, p. 31. **8.** I. M. Cohen, Discussant, **ibid.**, p. 35. **9.** G. A. Constant, **ibid.**, p. 37. **10.** L. J. Thomas, **ibid.**, p. 40. **11.** R. C. V. Robinson, **ibid.**, p. 43. **12.** S. C. Kaim and I. N. Rosenstein, **ibid.**, p. 46. **13.** H. E. Ticktin and J. D. Schultz, **ibid.**, p. 49. **14.** J. N. Sussex, **ibid.**, p. 53. **15.** I. N. Rosenstein, **ibid.**, p. 57. **16.** D. C. English, **Curr. Therap. Res., 2**:88, 1960. **17.** T. H. Harris, **J.A.M.A., 172**:1162, 1960.

T.M. Hydrochloride—7-chloro-2-methylamino-5-phenyl-3H-1,4-benzodiazepine 4-oxide hydrochloride

ROCHE
LABORATORIES
of Hoffmann-La Roche Inc.

NO SPRAIN, NO STRAIN, OR LOW BACK PAIN

can resist the rapid relaxant relief of

RELA™

CARISOPRODOL

RELA—SCHERING'S MYOGESIC[x]
RELAXES MUSCLE TENSION
FOR MORE ADEPT MANAGEMENT
OF BOTH SPASM AND ITS PAIN

Rela is most useful in the areas where narcotic analgesics are unwarranted and where salicylates are inadequate. Its muscle-relaxant properties are dependable yet significantly free of the limitations or problems often associated with other relaxants.

[x] **MYOGESIC:** MUSCLE RELAXANT ANALGESIC

Rela relaxes acute muscle spasm
Relief of muscle spasm (excellent to good effectiveness in the majority of patients).[1]

Rela provides persistent pain relief through its relaxant and analgesic actions
"Relief from pain was usually rapid and sometimes dramatic."[1]

Rela provides comfort free of spasm and pain
"A number of patients reported freedom from insomnia which they attributed to freedom from pain."[1]

1. Kuge, T.: To be published.

Schering

M-247

the indication: prostatitis

the incidence: "amazingly high"—"Inflammations of the prostate gland...occur with an amazingly high incidence in general practice."

the inference: probably "the most common chronic infection in men over 40 years of age."

Palliate TERMINAL CANCER with DILAUDID®

(DIHYDROMORPHINONE HCl.)

by mouth • by needle • by rectum

Nearly three decades of use and 500 million administered doses assure a predictable response with DILAUDID: rapid onset, long-lasting analgesia with less euphoria, less drowsiness, less constipation, less nausea and vomiting than morphine. DILAUDID, an opiate, is subject to Federal narcotic regulations, and usual precautions should be observed.

A dosage form for every need: Soluble tablets—1, 2,* 3 and 4 mg. (for oral or hypodermic use) • Rectal suppositories—2.7 mg. • Ampules—2,* 3 and 4 mg. • Powder • Multiple dose vials

**Average dose*

DILAUDID® E. Bilhuber, Inc.

For acute comments on chronic disorders, read FOCUS

DILAUDID
belongs in your bag

KNOLL PHARMACEUTICAL COMPANY, Orange, New Jersey

IN EPISTAXIS

"PREMARIN" INTRAVENOUS

the physiologic hemostat

ARRESTS BLEEDING PROMPTLY & SAFELY

Ayerst®

AYERST LABORATORIES

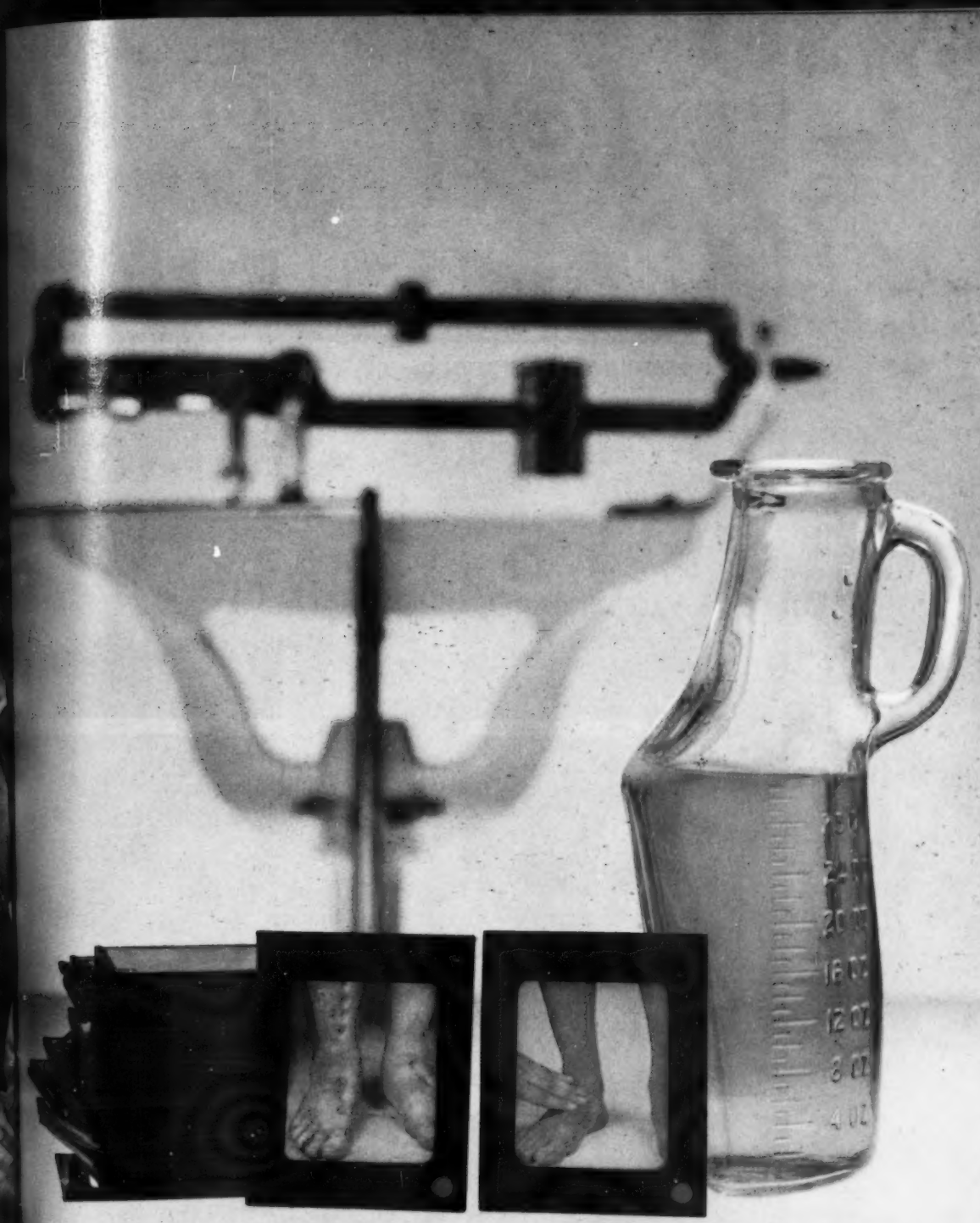
New York 16, N.Y. • Montreal, Canada

A single injection of "PREMARIN" INTRAVENOUS was effective in over 90 per cent of 641 cases of epistaxis — usually within 20 to 60 minutes.[2]

Over 1,000,000 injections have been given to date without a single report of toxicity or production of thrombi — in control of spontaneous hemorrhage and suppression of bleeding during and after surgery of every type.

"PREMARIN" INTRAVENOUS (conjugated estrogens, equine) is supplied in packages containing one "Secule"® providing 20 mg., and one 5 cc. vial sterile diluent with 0.5% phenol U.S.P.

1. Johnson, J. F. Paper presented at Symposium on Blood, Wayne State University, Detroit, Michigan, Jan. 18, 1957; cited in M. Science 1:33 (Mar. 25) 1957; Proc. Soc. Exper. Biol. & Med. **94**:92 (Jan.) 1957. 2. Published and unpublished case reports, Ayerst Laboratories. 3. Jacobson, P.: Virginia M. Month. **85**:548 (Oct.) 1958; West. J. Surg. **63**:711 (Dec.) 1955. 4. Rigg, J. P.: Digest Ophth. & Otolaryng. **20**:28 (Nov.) 1957. 5. Rigual, R.: Ibid., p. 3. 6. Menger, H. C.: J.A.M.A. **159**:546 (Oct. 8) 1955.



you get these results in case after case of edema and hypertension with **ESIDRIX®**

hospitalized patient with congestive heart failure

5 pounds lost in 4 days; 4+ pitting cleared; hepatic congestion and râles cleared; patient ambulatory

office patient treated for pedal edema and persistently high diastolic pressure

blood pressure reduced from 214/110 to 180/94 mm. Hg within 7 days with Esidrix (and Singoserp); pitting edema cleared

private patient with congestive heart failure; ascites and 4+ edema to the knee

12½ pounds lost in 13 days; basilar râles and ascites no longer present; pitting edema of legs and feet cleared

hospitalized patient with Laennec's cirrhosis

27 pounds lost in 19 days; abdominal swelling and pedal edema cleared

Photos used with permission of the patients

here is how patient
after patient with
edema and hypertension
responds to

ESIDRIX®

(hydrochlorothiazide CIBA)

- Esidrix, the improved analog of chlorothiazide, produces the highest fluid yields, the lowest blood pressure levels so far achieved with oral diuretics
- Esidrix relieves edema in certain patients refractory to other diuretics*
- Esidrix markedly increases sodium and chloride excretion, but its effect on potassium excretion is minimal
- Esidrix is exceptionally well tolerated

*Brest, A. N., and Likoff, W.: Am. J. Cardiol. *3*:144 (Feb.) 1959.

CIBA
SUMMIT, NEW JERSEY

In hospitals, clinics, and in the office…case after case of congestive heart failure
hypertension
hypertensive vascular disease
premenstrual edema
edema of pregnancy
steroid-induced edema
edema of obesity
nephrosis

responds to **ESIDRIX®**

(hydrochlorothiazide CIBA)

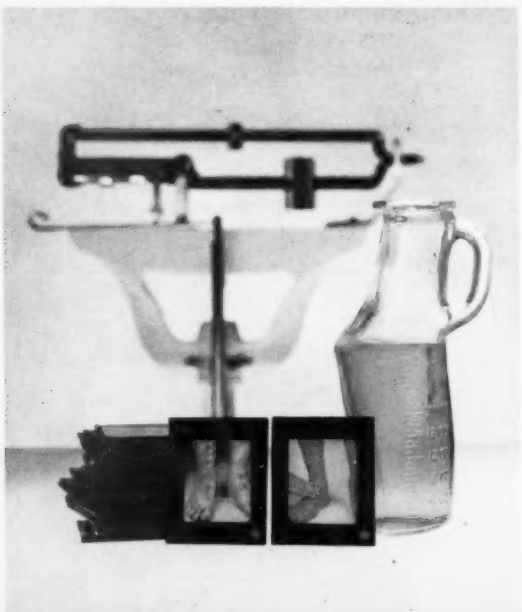
A PRODUCT OF CIBA RESEARCH

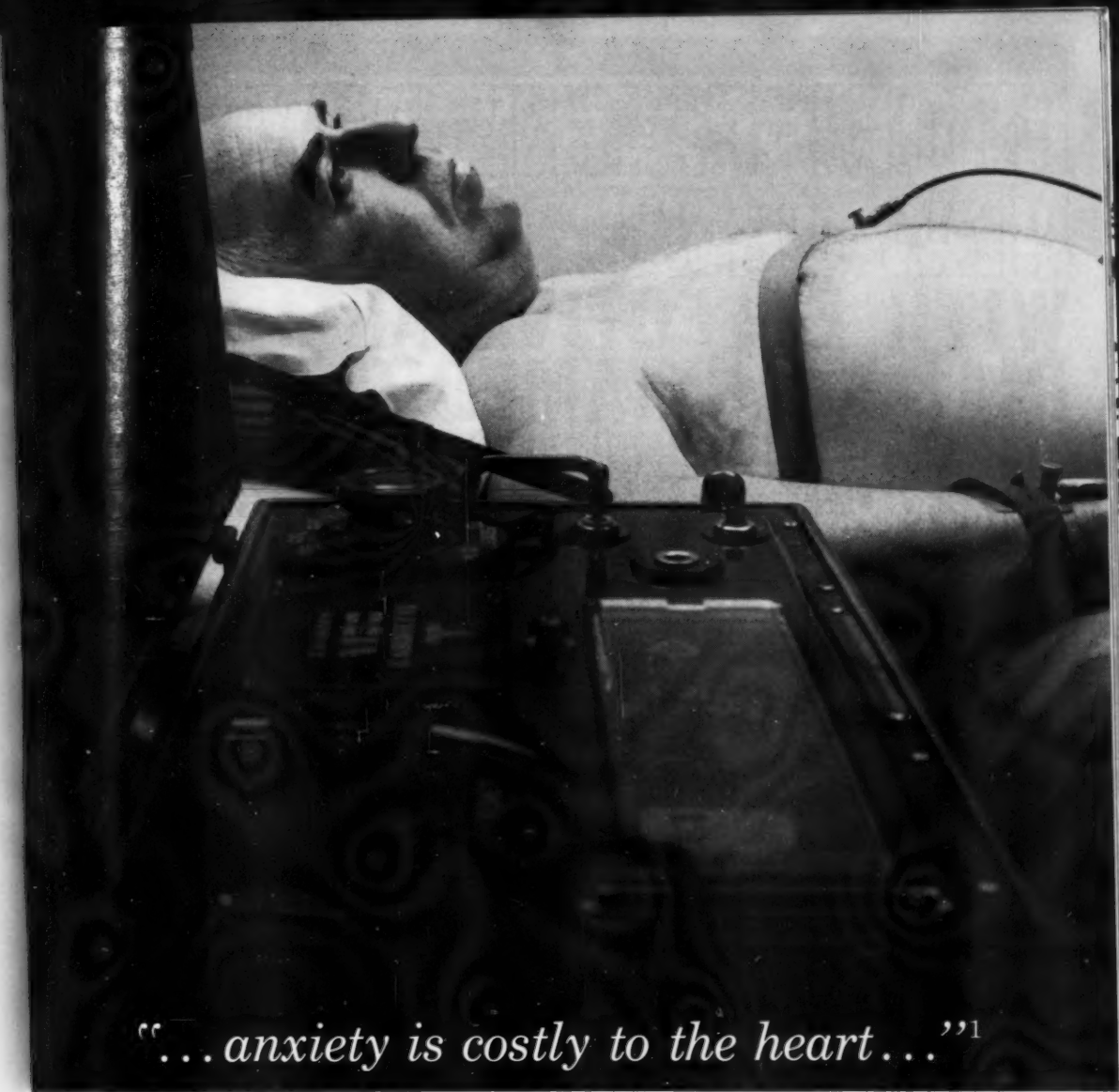
SUPPLIED: Esidrix *Tablets*, 25 mg. (pink, scored) and 50 mg. (yellow, scored). Complete information available on request.

SINGOSERP® (syrosingopine CIBA)
SERPASIL® (reserpine CIBA)

2/2802MK

CIBA
SUMMIT, NEW JERSEY





"...anxiety is costly to the heart..."[1]

"In at least 80 per cent of the patients seen by the cardiologist, anxiety prolongs and intensifies the physical disorder. For ambulatory patients, meprobamate is believed most suitable of the ataractic agents [to control anxiety]."[2]

The efficacy and wide safety margin of EQUANIL (meprobamate, Wyeth) is attested to by hundreds of published clinical studies. EQUANIL is predictable in its effects; pharmacologic actions are not diffuse. EQUANIL is well tolerated. Effects are not cumulative even on prolonged use. Side-reactions are remarkably few and mild.

Although rare, allergic reactions may occur; excessive dosage should be avoided in all patients. For further information on prescribing and administering EQUANIL see descriptive literature, available on request.

Wyeth Laboratories Philadelphia 1, Pa.

1. *Waldman, S., and Pelner, L.: Am. Pract. & Digest Treat. 8:1075 (July) 1957.*
2. *Friedlander, H.S.: Am. J. Cardiology 1:395 (March) 1958.*

Equanil®
Meprobamate, Wyeth

100 ANNIVERSARY Wyeth®
A Century of Service to Medicine

FROM PARKE-DAVIS...A NEW ORAL ANTIBIOTIC

WITH EFFECTIVE ANTIBACTERIAL & ANTIAMEBIC ACTIONS

"THE FORTUNATE COMBINATION OF HIGH ANTIAMEBIC AND ANTIBACTERIAL ACTIVITY AND LOW ORAL TOXICITY MAKES PAROMOMYCIN UNIQUE AMONG THE AVAILABLE DRUGS AND SUGGESTS THAT IT SHOULD BE A USEFUL THERAPEUTIC SUBSTANCE."[1]

● **IN INFECTIOUS DIARRHEAS**[2-5] Because it is effective against gram-negative pathogens, HUMATIN has proved especially valuable in infectious diarrheas, most of which are caused by bacilli of the gram-negative group. In 221 patients with severe diarrhea, 85 per cent obtained rapid remission of symptoms with HUMATIN, and stools cleared quickly of pathogens.[2] Results in *Shigella* and *Salmonella* enteritis,[5] and in infantile diarrheas of mixed etiology[3] have been uniformly good.

● **IN INTESTINAL AMEBIASIS**[2,5-8] HUMATIN is unusually effective in clearing all phases of intestinal amebiasis;[5] to date, more than 700 patients have been treated successfully with HUMATIN in all parts of the world. Since HUMATIN is not appreciably absorbed from the gastrointestinal tract it is not effective against extraintestinal forms of amebiasis.

Hum

ALSO VALUABLE IN THE PREOPERATIVE SUPPRESSION OF INTESTINAL FLORA,[2] AND IN THE ADJUNCTIVE MANAGEMENT OF HEPATIC COMA [9-11]

ADMINISTRATION AND DOSAGE

(expressed in terms of base)

Condition	Dosage (daily, in divided doses)	Duration of Therapy
Infectious Diarrheas (bacillary and nonspecific)	*Adults:* 35 to 50 mg/Kg; up to 100 mg/Kg in severe cases.	Up to 7 days
	Children: 50 mg/Kg; up to 100 mg/Kg in severe cases.	Up to 7 days
Intestinal Amebiasis (acute, subacute, chronic)	*Adults:* 0.75 to 1.5 Gm.; larger doses when required.	5 days
	Children: 22 mg/Kg; larger doses when required.	5 days
Preoperative Suppression of Intestinal Flora	*Adults:* 2 Gm.	4 days
Hepatic Coma	*Adults:* up to 6 Gm., depending on degree of hepatic insufficiency and response of patient.	See literature

SIDE EFFECTS: Since HUMATIN by the oral route is virtually nonabsorbed in the gastrointestinal tract, even with exceptionally high doses, systemic toxicity has not been a problem in clinical use.[2,3,5-8] However, when doses in excess of 2 Gm. per day are given for more than three days, loose stools may develop; on doses of from 4 to 6 Gm. daily, moderately severe diarrhea has been reported in some patients. No other indications of toxicity have been observed.

SUPPLIED: HUMATIN (paromomycin, Parke-Davis) is available as the sulfate in Kapseals,® each containing 250 mg. of base, in bottles of 16. Literature supplying details of dosage and administration available on request.

REFERENCES: (1) Coffey, G. L., *et al.*: *Antibiotics & Chemother.* **9**:730, 1959. (2) Personal Communications to the Department of Clinical Investigation, Parke, Davis & Company, 1959. (3) Godenne, G. D.: Paromomycin in diarrheas of infants and children, Antibiotics Annual 1959-1960, New York, Medical Encyclopedia Inc., in press. (4) McMath, W. F. T., & Hussain, K. K.: *Pub. Health* **73**:328, 1959. (5) Courtney, K. O., & Thompson, P. E.: Paromomycin as a therapeutic substance for intestinal amebiasis and bacterial enteritis, Antibiotics Annual 1959-1960, New York, Medical Encyclopedia Inc., in press. (6) Shafei, A. Z.: *Antibiotic Med. & Clin. Therapy* **6**:275, 1959. (7) Elias, F. L., & Oliver-Gonzales, J.: *Antibiotic Med. & Clin. Therapy* **6**:584, 1959. (8) Carter, C. H.: *Antibiotic Med. & Clin. Therapy* **6**:586, 1959. (9) Fast, B. B., *et al.*: *Arch. Int. Med.* **101**:467, 1958. (10) Mackie, J. E., *et al.*: *New England J. Med.* **259**:1151, 1958. (11) Stormont, J. M., *et al.*: *New England J. Med.* **259**:1145, 1958.

31760

PARKE, DAVIS & COMPANY · DETROIT 32, MICHIGAN PARKE-DAVIS

KAPSEALS®

atin®

(PAROMOMYCIN, PARKE-DAVIS)

"All my surgical patients get an extra lift with 'Beminal' Forte"

pre- and post-op to improve nutrition ...aid tissue repair

BEMINAL FORTE

Therapeutic B Factors with Vitamin C

A single capsule provides 250 mg. of vitamin C and massive doses of B factors to meet the need when requirements are high and reserves are low. Prescribe "Beminal"® Forte pre- and post-operatively, during convalescence, and for patients on special diets to improve the prognosis and accelerate recovery.

Supplied: No. 817 – Bottles of 100 and 1,000 capsules.

Ayerst Laboratories New York 16, N. Y. • Montreal, Canada

6010

The Pregnant

– and a natural way to meet her special need for calcium
– with low-calorie Carnation Instant

Drinking enough milk during pregnancy to assure sufficient calcium has posed the problem of unwanted fat calories – till recently.

Now a *natural* way to help assure your patients' good calcium and nutritional status is the excellent new food – *new Carnation Instant Nonfat Dry Milk mixed 25% overstrength.*

One-third cup extra crystals per liquid quart when mixing provides 25% more calcium, protein, and B-vitamins than ordinary nonfat milk. Because your patients can add this additional amount of Carnation Instant Nonfat, they get *needed* nutrition – *without* excessive calories. Its richer, more delicious flavor is a *natural* way to *extra* nutrition they will enjoy. Costs them only 10¢ a quart.

ANOTHER QUALITY PRODUCT OF CARNATION COMPANY. LOS ANGELES 36. CALIFORNIA

your Hypertensives: keep them awake & working

. . . and do the job with one prescription

Remarkably effective in the widest range of clinical applications

FOR PAIN

NUMORPHAN®

SUBCUT., I.M., AND RECTAL

In a series[1] of more than 500 consecutive deliveries: "There have been no untoward side effects noted in the mothers, and the incidence of respiratory depression in the infants has been almost negligible, comparing most favorably with other agents."

"There can be little doubt of the efficacy of Numorphan for the control of pain . . ."[2]

1. Sattenspiel, E.: Personal communication. 2. Samuels, M. L.; Stehlin, J. S.; Dale, S. C., and Howe, C. D.: South. M. J. 52:207, 1959.

A NEW ERA IN PAIN RELIEF

clinically tested for 5 years/evaluated in 120 U. S. hospitals/over a quarter of a million doses given/ more than 25,000 patients treated

For Literature on Numorphan, Write

ENDO LABORATORIES
Richmond Hill 18, New York

Endo

*U. S. PAT. 2,806,033

Clinical indications for NUMORPHAN

All conditions in which potent analgesia is required, such as:

DURING LABOR

before and after surgery

neoplastic diseases

gastrointestinal, renal, and biliary tract pain

orthopedic manipulations

severe burns and trauma

coronary occlusion with myocardial infarction

pleuritic pain

tabetic crises

radiculitis and other neurologic disorders

Note: Because it possesses little or no cough-inhibiting effect, NUMORPHAN* is the drug of choice for the patient who requires analgesia but must cough.

Available in 1 and 2 cc. ampuls and 10 cc. multiple-dose vials, 1.5 mg. /-14-hydroxydihydromorphinone hydrochloride per cc.; rectal suppositories, 2 mg. and 5 mg. May be habit-forming.

Tofrānil®

brand of imipramine HCl

in depression

lights the road to recovery in 80 per cent of cases

In the treatment of depression Tofrānil has established the remarkable record of producing remission or improvement in approximately 80 per cent of cases.[1-7]

Tofrānil is well tolerated in usage—is adaptable to either office or hospital practice—is administrable by either oral or intramuscular routes.

Tofrānil
a potent thymoleptic . . .
not a MAO inhibitor.

Does act effectively in *all* types of depression regardless of severity or chronicity.

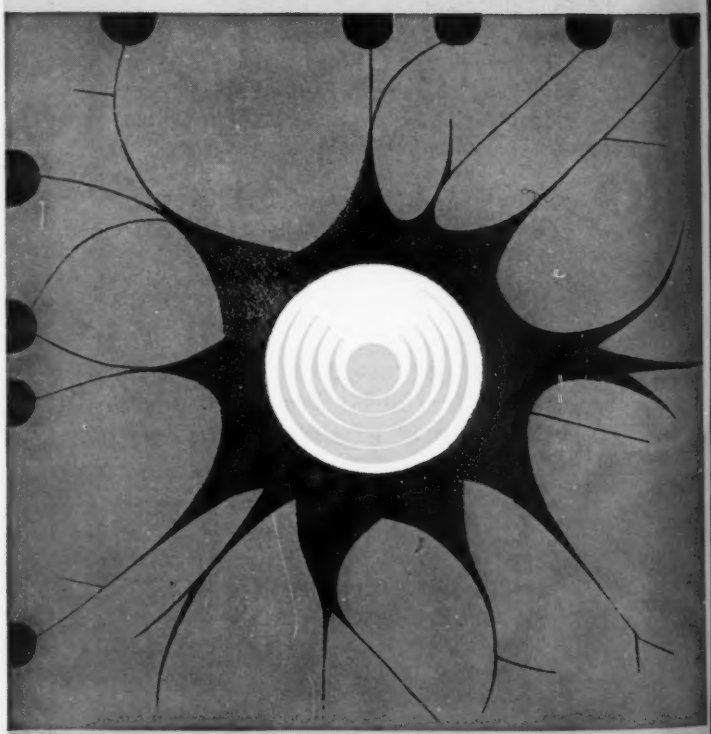
Does not inhibit monoamine oxidase in brain or liver; produce CNS stimulation; or potentiate other drugs such as barbiturates and alcohol.

Detailed Literature Available on Request.

Tofrānil® (brand of imipramine HCl), tablets of 25 mg., bottles of 100. Ampuls for intramuscular administration only, each containing 25 mg. in 2 cc. of solution, cartons of 10 and 50.

References: 1. Ayd, F. J., Jr.: Bull. School Med. Univ. Maryland *44*:29, 1959. 2. Azima, H., and Vispo, R. H.: A. M. A. Arch. Neurol. & Psychiat. *81*:658, 1959. 3. Lehmann, H. E.; Cahn, C. H., and de Verteuil, R. L.: Canad. Psychiat. A. J. *3*:155, 1958. 4. Mann, A. M., and MacPherson, A. S.: Canad. Psychiat. A. J. *4*:38, 1959. 5. Sloane, R. B.; Habib, A., and Batt, U. E.: Canad. M. A. J. *80*:540, 1959. 6. Straker, M.: Canad. M. A. J. *80*:546, 1959. 7. Strauss, H.: New York J. Med. *59*:2906, 1959.

Geigy, Ardsley, New York



Geigy

TO 4-60

FREEDOM FROM ANGINAL ATTACKS

24 HOURS OF UNINTERRUPTED PROTECTION

WITH ONE TEMPULE®
MORNING AND NIGHT

PENTRITOL®
TEMPULES
controlled disintegration
capsules

The best has been improved. PETN, proven over the years to be the most effective drug for preventing anginal attacks, has been improved by incorporating it into controlled disintegration capsules. Pentritol Tempules exhibit the benefits of PETN "...plus a smooth sustained clinical result that seemed to show a superior effect."[1]

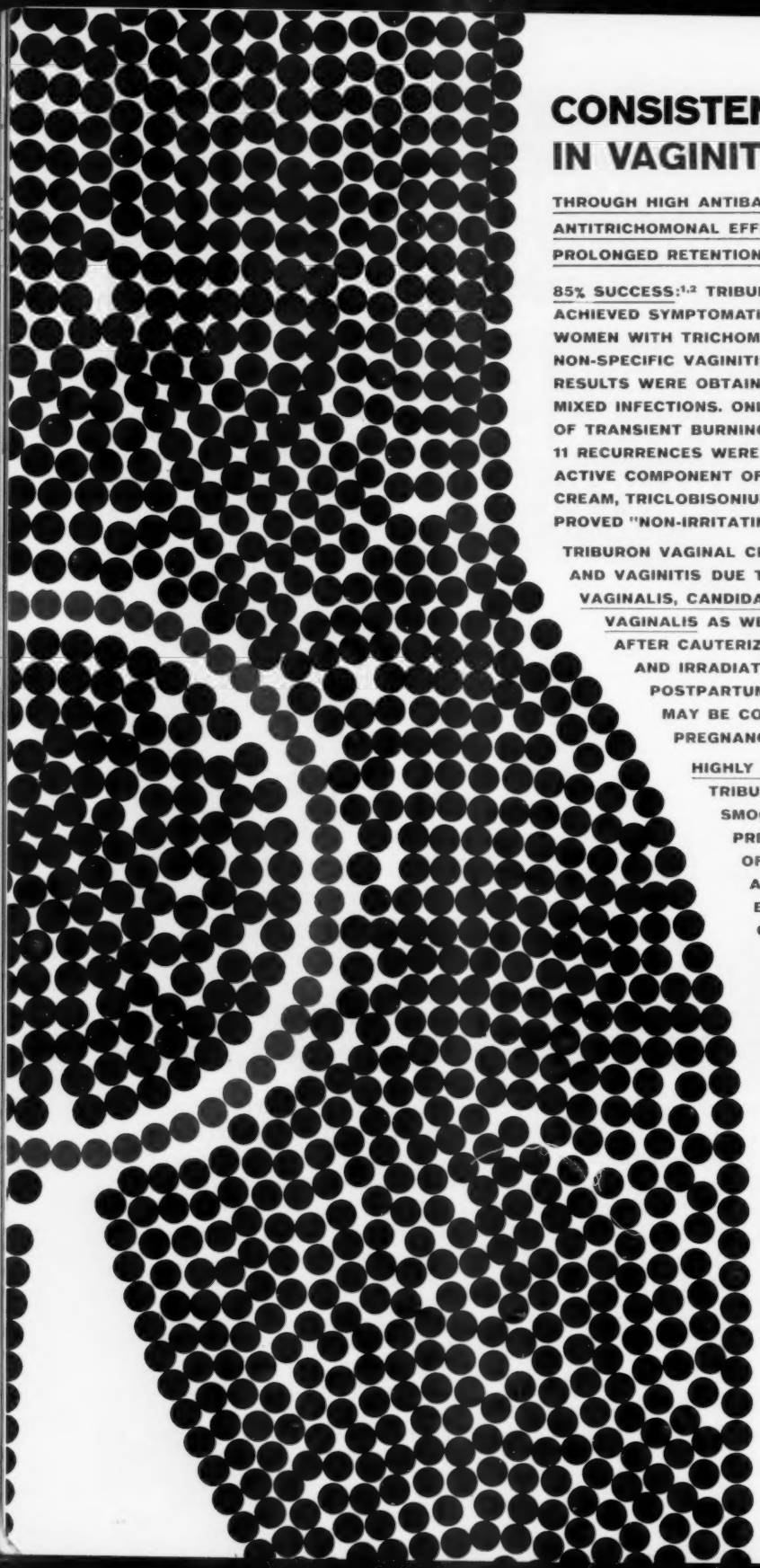
Pentritol Tempules given every 12 hours reduced or eliminated nitroglycerin requirements, stopped anginal attacks or reduced their frequency, eliminated or mitigated pain, and increased the capacity for physical activity. *Patients previously taking PETN in tablets with little progress, responded favorably to Pentritol Tempules.*[2]

Recommended dose is 1 Pentritol Tempule morning and evening, approximately 12 hours apart. Available in bottles of 60 Tempules. Also available: Pentritol-B Tempules with 50 mg. of butabarbital added for vasodilation *plus* sedation.

1. Biegeleisen, H. I.: Clin. Med. 2:1005, 1955. 2. Roberts, J. T.: Clin. Med. 4:1375, 1957.

©1960, A.P.Co.

ARMOUR PHARMACEUTICAL COMPANY • KANKAKEE, ILLINOIS *Armour Means Protection*



CONSISTENT RESPONSE IN VAGINITIS

THROUGH HIGH ANTIBACTERIAL AND ANTITRICHOMONAL EFFECTS, RAPID DIFFUSION, PROLONGED RETENTION

85% SUCCESS:[1,2] TRIBURON VAGINAL CREAM ACHIEVED SYMPTOMATIC CONTROL IN 109 OF 128 WOMEN WITH TRICHOMONAL, MONILIAL AND NON-SPECIFIC VAGINITIS. PARTICULARLY GOOD RESULTS WERE OBTAINED IN TRICHOMONAL AND MIXED INFECTIONS. ONLY TWO INSTANCES OF TRANSIENT BURNING OCCURRED, AND ONLY 11 RECURRENCES WERE NOTED. FURTHER, THE ACTIVE COMPONENT OF TRIBURON VAGINAL CREAM, TRICLOBISONIUM CHLORIDE, HAS BEEN PROVED "NON-IRRITATING...NOT SENSITIZING."[3]

TRIBURON VAGINAL CREAM—FOR VULVITIS AND VAGINITIS DUE TO TRICHOMONAS VAGINALIS, CANDIDA ALBICANS, HEMOPHILUS VAGINALIS AS WELL AS MIXED INFECTIONS; AFTER CAUTERIZATION, CONIZATION AND IRRADIATION; FOR SURGICAL AND POSTPARTUM TREATMENT. THERAPY MAY BE CONTINUED DURING PREGNANCY AND MENSTRUATION.

HIGHLY ACCEPTABLE TO PATIENTS TRIBURON VAGINAL CREAM—A SMOOTH, WHITE, NONSTAINING PREPARATION WITH NO HINT OF MEDICINAL ODOR—HAS THE ADVANTAGES OF CONVENIENT BEDTIME ADMINISTRATION AND OF DISPOSABLE APPLICATORS.

SUPPLIED: 3-OUNCE TUBE WITH 18 DISPOSABLE APPLICATORS.

REFERENCES: 1. N. MULLA AND J. J. McDONOUGH, ANN. NEW YORK ACAD. SC., 82:(ART. 1), 182, 1959. 2. L. E. SAVEL, D. B. GERSHENFELD, J. FINKEL AND P. DRUCKER, IBID., P. 186. 3. R. C. V. ROBINSON AND L. E. HARMON, ANTIBIOTICS ANNUAL 1958-1959, NEW YORK, MEDICAL ENCYCLOPEDIA, INC., 1959, P. 113.

TRIBURON® CHLORIDE

ROCHE LABORATORIES
DIVISION OF HOFFMANN-LA ROCHE
NUTLEY 10, N. J.

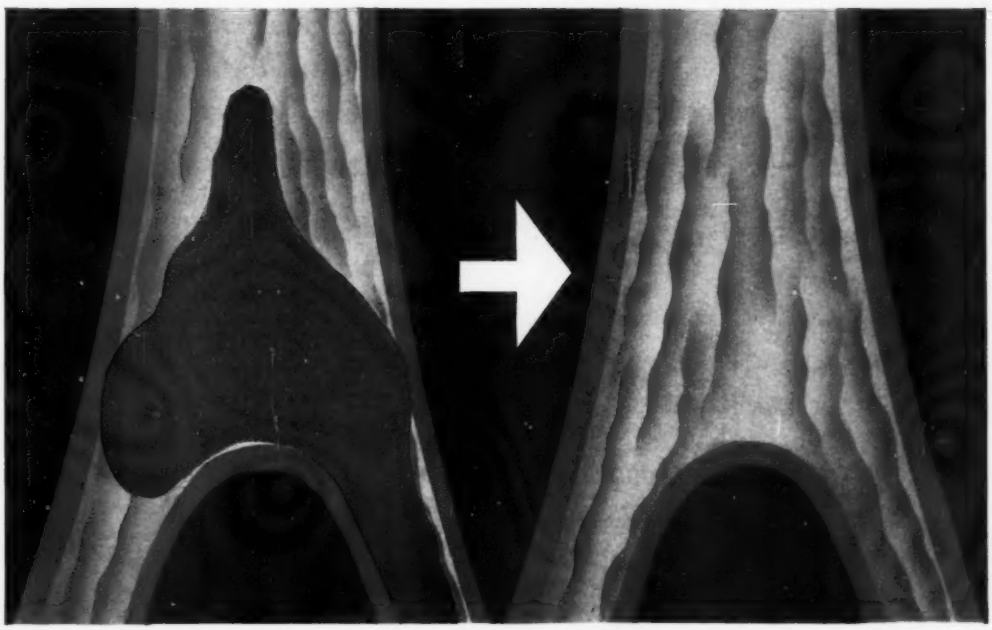
Triburon
VAGINAL CREAM
decisive microbicidal therapy
in a delicate matter
not an antibiotic • not a nitrofuran

clinical endorsement grows as proof accumulates

ACTASE
TRADEMARK

Fibrinolysin (Human)

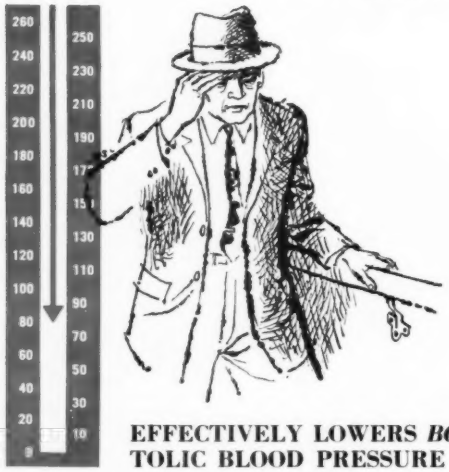
NOT JUST A NEW DRUG... *A NEW THERAPY*



Ortho

SPECIFIC FOR THE DISSOLUTION
OF INTRAVASCULAR CLOTS

New flexible, predictable therapy in essential hypertension



EFFECTIVELY LOWERS *BOTH* SYSTOLIC AND DIASTOLIC BLOOD PRESSURE

OSTENSIN produces prompt and prolonged sympathetic blockade. Systolic *and* diastolic blood pressure are smoothly and predictably reduced.

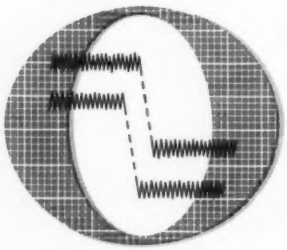
ALSO FOR FLEXIBLE ADJUNCTIVE USE

Concomitant use of the newer oral diuretics such as chlorothiazide and its derivatives[1,2] allows reduction in dosage, flexibility in regimen.

FEWER, MILDER BY-EFFECTS

Virtual absence of constipation.[3] Certain other by-effects common to most ganglionic blocking agents occur less frequently and are less pronounced.[1,3,4,5]

TABLETS



Keystone in a New Antihypertensive Regimen

Ostensin®

OSTENSIN is the registered trademark for Trimethidinium Methosulfate, Wyeth

Wyeth Laboratories Philadelphia 1, Pa.

Supplied: Tablets, scored 20 and 40 mg., vials of 100.

For further information on prescribing and administering OSTENSIN see descriptive literature, available on request.

References: 1. Smirk, F.H.: Am. Heart J. *58*:701 (Nov.) 1959. 2. Janney, J.G., Jr., et al.: Am. J. Cardiology *4*:745 (Dec.) 1959. 3. Dunsmore, R.A., et al.: Am. J.M. Sc. *236*:483 (Oct.) 1958. 4. Blaquier, P., et al.: Univ. Michigan M. Bull. *24*:309 (Oct.) 1958. 5. Borhani, N.O.: Ann. Int. Med. *51*:983 (Nov.) 1959.

A Century of Service to Medicine

all of these patients have anxiety symptoms;

*but <u>half</u> need an antidepressant, not a tranquilizer

depression–a common problem in office practice...

"It is generally acknowledged that at least 40 to 50 per cent of the patients seen in private practice have emotional problems and that true depressions or depressive equivalents are found in more than half of these." Cooper, J. H.: J. Am. M. Women's A. *14*:988, 1959

anxiety often "masks" underlying depression...

"Although ataractics have a definite place in therapeutics, their use in depressed states is limited, and in many cases even contraindicated. A large number of patients with psychogenic disorders are given ataractics for the relief of anxiety symptoms. Since the anxiety is actually due to depression, the response, if any, is transient and occasionally the patient may become worse...." Hobbs, L. F.: Virginia M. Month. *86*:692, 1959

IN DEPRESSION AND DEPRESSION-INDUCED ANXIETY

the common problems basically unresponsive to tranquilizers

Nardil®

brand of phenelzine dihydrogen sulfate

relieves the anxiety by removing the depression itself

dosage: One tablet three times a day.

supplied: Orange-coated tablets, each containing 15 mg. of phenylethylhydrazine present as the dihydrogen sulfate. Bottles of 100.

Complete Nardil Bibliography on request to the Medical Department.

WARNER CHILCOTT
MORRIS PLAINS, N.J.

NA-6F04

Arterial representation adapted from Recueil de Planches, Tome Second, Chez Pellet, a Geneve, 17

ECONOMICAL 1-TABLET-A-DAY SALUTENSIVE

saluron

sustained-action hydroflumethiazide 'Bristol'

For a salutary lowering of high blood pressure

an effective salutensive agent

saluretic and antihypertensive

SALURON™

sustained-action hydroflumethiazide 'Bristol'

As an antihypertensive:

"a distinct advantage in the manifestations of hypertension"[1]

...a superior foundation drug (hydroflumethiazide) for an antihypertensive regimen ... often the only drug required for effective therapy.[1,2]

...in other cases, enhances the antihypertensive effects of concurrently administered tranquilizers and ganglionic blockers (usually permitting smaller dosage).[1,2,3]

...helps to restore "dry weight" while lowering blood pressure.[1]

As a saluretic:

"a marked advancement in the field of diuretic therapy"[4]

...prompt sodium excretion,[1-6] with "a duration of at least 18 hours" on a single 50-mg. tablet.[1]

...less potassium and bicarbonate excretion or pH change than with chlorothiazide or hydrochlorothiazide.[1,4,5,7,8,9,11,12]

...well tolerated[1,3,4,5,6,12] ..."repetitively effective."[1,7]

INDICATIONS: *Hypertension and hypertensive cardiovascular disease:* Saluron induces a gradual but sustained decrease in abnormally elevated blood pressure—both systolic and diastolic. It has no significant effect on normal blood pressure. Saluron may be used successfully in conjunction with other antihypertensive agents.

Edema: associated with cardiac or renal insufficiency, hepatic cirrhosis, pregnancy, premenstrual syndrome, or steroid administration.

DOSAGE: Usually 1 tablet daily. Full information in package insert.

SUPPLY: Scored 50-mg. tablets; bottles of 50. Syrup, containing 50 mg. per 5-ml. teaspoonful; bottles of 8 fl. oz.

Bristol

BRISTOL LABORATORIES, SYRACUSE, N.Y.

Division of Bristol-Myers Co.

...FERENCES:
...ford, R. V., and Nickell, ...Int. Med. & Clin. Ther. ...1959. 2. Cohen, B. ...Current Therap. Res. ...1959. 3. Blagg, C. R.: ...ncet 2:311, 1959. 4. ...s, M., and Mallin, S. ...t. Red. Med. 172:438, ...5. Edmonds, C. J., ...Wilson, G. M.: Lancet ...1959. 6. Kennedy, ... Watson, W. C., and ...ngham, C.: Lancet 2: ...1959. 7. Ford, R. V.: ... Rac. Med. 172:434, ...8. Fuchs, M., Mallin, ... and Moyer, J. H.: Cir... ...on 20:699, 1959. 9. ...g, D. S., Forrester, T. ... and Morgan, T. N.: ...nat. 2:765, 1959. 10. ...ttuschi, E.: Lancet 2: ...1959. 11. Foreign Let... J.A.M.A. 170:1864, ...12. Jones, J. H., and ... V.: British M. J. ...1959.

in musculoskeletal disorders

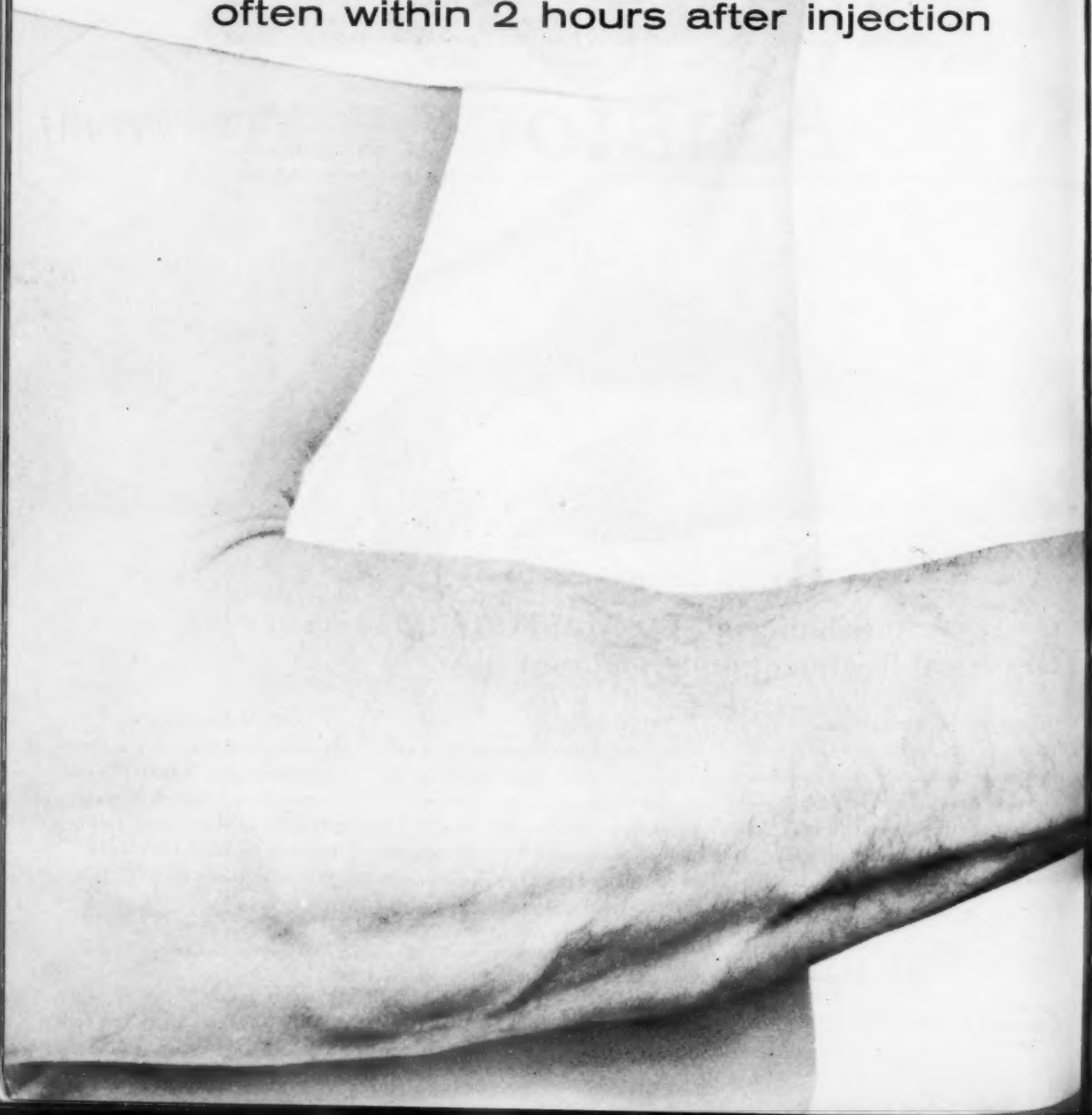
INJECTION

Decadron® PHOSPHATE

DEXAMETHASONE 21-PHOSPHATE

usually controls the acute phase

often within 2 hours after injection



THE DIRECT APPROACH — rapid relief and prolonged effect—complete solubility affords quick diffusion of the therapeutic dose

THE DIRECT APPROACH — mg. for mg. the most active steroid

THE DIRECT APPROACH — passes easily through small-bore needles

THE DIRECT APPROACH — needs no reconstitution—no refrigeration

Injection DECADRON Phosphate can be used in strains and sprains, bursitis, fibrositis, rheumatoid arthritis, traumatic arthritis, acute gouty arthritis, osteoarthritis, osteochondritis, "trigger" points (localized painful areas in muscles), tendinitis, whiplash injuries (acute), and muscle trauma.

Caution: Steroids should not be given in the presence of tuberculosis, chronic nephritis, acute psychosis, peptic ulcer, or ocular herpes simplex.

Note: Do not inject into intervertebral joints.

DOSAGE AND ADMINISTRATION:
Injection DECADRON Phosphate is ready for immediate use intramuscularly or intra-articularly.
Dosage varies from 0.4 to 6 mg. or more depending on the nature and severity of the condition.

SUPPLIED:
5 cc. vials with 4 mg. dexamethasone 21-phosphate as the disodium salt per cc.

Additional information on Injection DECADRON Phosphate is available at your request.

DECADRON is a trademark of Merck & Co., Inc.

MSD MERCK SHARP & DOHME • Division of Merck & Co., Inc. • West Point, Pa.

anticholinergic

KEEPS THE STOMACH FREE OF PAIN

tranquilizer

KEEPS THE MIND OFF THE STOMACH

Milpath acts quickly to suppress hypermotility, hypersecretion, pain and spasm, and to allay anxiety and tension with minimal side effects.

AVAILABLE IN TWO POTENCIES:

Milpath-400 – Yellow, scored tablets of 400 mg. Miltown (meprobamate) and 25 mg. tridihexethyl chloride. Bottle of 50.

Dosage: 1 tablet t.i.d. at mealtime and 2 at bedtime.

Milpath-200 – Yellow, coated tablets of 200 mg. Miltown (meprobamate) and 25 mg. tridihexethyl chloride. Bottle of 50.

Dosage: 1 or 2 tablets t.i.d. at mealtime and 2 at bedtime.

Milpath®

®Miltown + *anticholinergic*

WALLACE LABORATORIES *New Brunswick, N. J.*

GENTLE STIMULUS...FOR POSITIVE RESULTS

PERI-COLACE

Dioctyl sodium sulfosuccinate and anthraquinone derivatives from cascara. Mead Johnson

in management of constipation

Peri-Colace induces prompt, positive, yet gentle results in constipation through the synergistic action of its ingredients:

1. Peristim,® a mild laxative, "...exerts its peristaltic stimulating action directly on the large intestine, via the blood stream."[1]

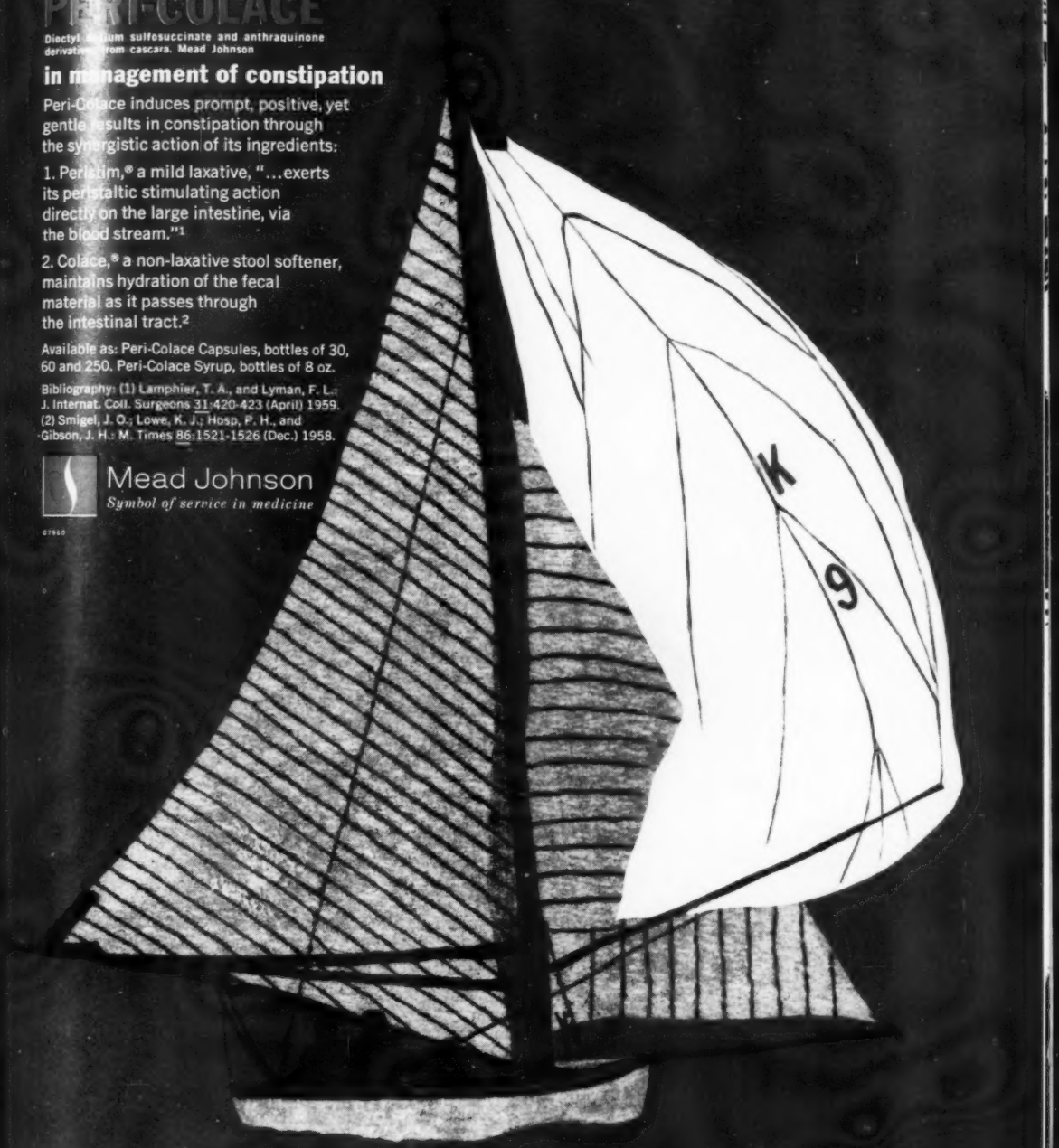
2. Colace,® a non-laxative stool softener, maintains hydration of the fecal material as it passes through the intestinal tract.[2]

Available as: Peri-Colace Capsules, bottles of 30, 60 and 250. Peri-Colace Syrup, bottles of 8 oz.

Bibliography: (1) Lamphier, T. A., and Lyman, F. L.: J. Internat. Coll. Surgeons 31:420-423 (April) 1959. (2) Smigel, J. O.; Lowe, K. J.; Hosp, P. H., and Gibson, J. H.: M. Times 86:1521-1526 (Dec.) 1958.

Mead Johnson
Symbol of service in medicine

07960



Technical Exhibits — In Print

Abbott Laboratories—Selsun; Iberol ... Facing A-16-17
Vitamins ... Facing A-64-65
Desoxyn ... A-122-123
Oreticyl ... A-186-187
American Meat Institute ... A-64
Ames Company, Inc.—Decholin ... A-33
Armour Pharmaceutical Company
Chymoral ... A-24
Pentritol ... A-197
Ayerst Laboratories—Timovan ... A-34-35
Premarin Intravenous ... A-180
Beminal ... A-184
Bristol Laboratories, Inc.—Naldecon ... A-41
Saluron ... A-202-203
Burroughs Wellcome & Company, Inc.
Cortisporin; Neosporin; Polysporin ... A-161
Carnation Company—Evaporated Milk ... A-14
Instant Milk ... A-185
Ciba Pharmaceutical Products, Inc.
Serpasil-Esidrix ... A-51
Doriden ... A-68-69
Serpasil ... A-129
Esidrix ... Facing A-180-181
Serpasil-Apresoline ... Fourth Cover
Davies, Rose & Co., Ltd.—Quinidine Sulfate ... A-211
Desitin Chemical Company—Ointment ... A-13
Eastman Kodak Company ... Facing A-148-149
Eaton Laboratories—Altafur ... A-79
Furadantin ... A-170-171
Endo Laboratories, Inc.—Coumadin ... A-58
Numorphan ... A-191
Fleet, C. B., Company, Inc.—Enema ... A-120
Florida Citrus Commission ... A-48
Fougera, E., & Co., Inc.—Digitaline Nativelle ... A-134
Geigy Pharmaceuticals—Anturan ... A-25
Hygroton ... A-93
Butazolidin ... A-177
Tofranil ... A-192
Gomco Surgical Mfg. Corporation
Thermotic Drainage Pump ... A-189
Hyland Laboratories—TA-Test ... A-100
Knoll Pharmaceutical Company—Dilaudid ... A-179
Lakeside Laboratories, Inc.—Catron ... A-108
Caytine ... A-109
Lederle Laboratories—Gevral ... A-26-27
Filibon ... A-95
Pathibamate ... A-152-153
Neo-Aristoderm ... A-204-205
Declomycin ... A-212
Leeming, Thos., & Company—Metamine ... A-127
Lilly, Eli, & Company—En-Cebrin ... A-5
McNeil Laboratories, Inc.—Syndrox ... A-16
Paraflex ... A-136
Tylenol ... A-210
Mead Johnson & Company
Tacaryl ... Facing A-48-49; A-49
Vi-Sol ... A-80
Vasodilan ... A-131
Metrecal ... A-150-151
Natalins ... A-173
Peri-Colace ... A-209
Merck Sharp & Dohme, Div. Merck & Co., Inc.
Decadron ... Second Cover; A-206-207; Third Cover
Diuril ... A-30-31
Hydeltra-T.B.A. ... A-47
NeoDecadron ... A-104
Diupres ... A-118-119
Aramine ... A-146-147
Merrell, The Wm. S., Company—Bentyl ... A-28
Kolantyl ... A-84
MER/29 ... Facing A-132-133
Mulford Colloid Laboratories—Anergex ... A-91
Mutual Benefit Life Insurance Company, The ... A-165
Organon, Inc.—Durabolin ... A-57
Ortho Pharmaceutical Corp.—Diaphragms ... A-106
Actase ... A-199

Everything under control...including the temperature with

Tylenol

first liquid pediatric antipyretic/analges

"... a safe and effective agent [acetaminophen] in the control of fever at any age in contrast to other agents which are of known toxicity"[1]

Tylenol® *Acetaminophen*
brings fever and pain under control quickly safely ... well liked by children.

1. Mintz, A. A.: Management of the Febrile C... J. Ky. Acad. Gen. Pract. 5:26 (Jan.) 1...

Tylenol Elixir—120 mg. per 5 cc.

Tylenol Drops—60 mg. per 0.6 cc.

McNEIL

McNEIL LABORATORIES, INC.
Philadelphia 32, Pa.

Parke, Davis & Company—Dilantin A-15
Myadec A-89
Norlutin A-103
Benylin A-144
Chloromycetin A-162-163
Humatin A-182-183
Pfizer Laboratories, Div. Chas. Pfizer & Co., Inc.
Niamid A-102
Moderil A-105
Visteril A-148
Bonine A-158-159
Pitman-Moore Company—Phenoxene A-10
Purdue Frederick Company, The—Athrombin-K A-8
Senokot A-9
Riker Laboratories, Inc.—Disipal A-61
Medihaler-Ergotamine A-133
Robins, A. H., Co., Inc.—Dimetane A-12
Robaxin A-50
Pabalate A-121
Robaxisal A-142-143
Roche Laboratories, Div. Hoffmann-La Roche, Inc.
Triburon A-22-23-193
Alurate A-55
Azo Gantrisin A-65
Tigan A-99
Noludar A-125
Marplan A-140
Librium A-166-167
Madribon A-194-195
Roerig, J. B., and Company—Antivert A-53
Maxipen A-112-113
Sanborn Company—Electrocardiographs A-149
Sandoz Pharmaceuticals—Mellaril A-66-67
Saunders, W. B., Company—Medical Books A-17
Schering Corporation—Alpen A-36-37-38-39
Sigmagen A-78
Diloderm A-135-137-139-141
Rela A-168-169
Schmid, Julius, Inc.—Ramses A-60
Searle, G. D., & Co.—Pro-Banthine with Dartal . A-1
Sherman Laboratories—Elixophyllin A-32
Smith-Dorsey, Div. The Wander Company
Triaminic A-110-111
Squibb, E. R., & Sons, Div. Mathieson Chem. Corp.
Mysteclin-V A-19
Rubramin PC A-114-115
Strasenburgh, R. J., Company
Biphetamine; Ionamin A-101
Wallace Laboratories, Div. Carter Products, Inc.
Meprospan A-7
Deprol A-62-63
Milprem A-72
Miltrate A-87
Miltown; Soma ....A-116; Facing A-116-117; A-117
Miltown A-164
Milpath A-203
Warner-Chilcott Laboratories
Div. Warner-Lambert Pharmaceutical Co.
Mandelamine A-43
Pyridium A-45
Gelusil A-145
Nardil A-201
Warren-Teed Products Company, The
Ilopan-Choline A-81
White Laboratories, Inc.—Permitil A-21
Sorboquel A-154-155-156-157
Winthrop Laboratories—A.P.C. with Demerol .. A-2
Wyeth Laboratories—Zactirin A-29
Oxaine A-70-71
Equagesic ..... Facing A-84-85; A-85
Polymagma A-107
Aludrox A-132
Equanitrate A-138
Mepergan A-160
Phenergan A-175
Equanil A-181
Ostensin A-200

Of special significance to the physician is the symbol

When he sees it engraved on a Tablet of Quinidine Sulfate he has the assurance that the Quinidine Sulfate is produced from Cinchona Bark, is alkaloidally standardized, and therefore of unvarying activity and quality.

When the physician writes "DR" (Davies, Rose) on his prescriptions for Tablets Quinidine Sulfate, he is assured that this "quality" tablet is dispensed to his patient.

Rx Tablets Quinidine Sulfate Natural
0.2 Gram (or 3 grains)
Davies, Rose

Clinical samples sent to physicians on request

Davies, Rose & Company, Limited
Boston 18, Mass.

D-7

greater activity

unsurpassed G.I. toleration

sustained peak action

extra-day protection against relapse

NOW...THE EXTRA BENEFITS OF BROAD-SPECTRUM

DECLOMYCIN®

Demethylchlortetracycline Lederle

IN THE NEW, CHERRY-FLAVORED **SYRUP**

75 mg./5 cc. tsp., in 2 fl. oz. bottle—3-6 mg. per lb. daily in four divided doses

LEDERLE LABORATORIES, a Division of AMERICAN CYANAMID COMPANY, Pearl River, New York

CLINICAL REMISSION IN A "PROBLEM" ARTHRITIC

In rheumatoid arthritis with diabetes mellitus. A 54-year-old diabetic with a four-year history of arthritis was started on DECADRON, 0.75 mg./day, to control severe symptoms. After a year of therapy with 0.5 to 1.5 mg. daily doses of DECADRON, she has had no side effects and diabetes has not been exacerbated. **She is in clinical remission.***

New convenient b.i.d. alternate dosage schedule: the degree and extent of relief provided by DECADRON allows for b.i.d. maintenance dosage in many patients with so-called "chronic" conditions. Acute manifestations should first be brought under control with a t.i.d. or q.i.d. schedule.

Supplied: As 0.75 mg. and 0.5 mg. scored, pentagon-shaped tablets in bottles of 100. Also available as Injection DECADRON Phosphate. Additional information on DECADRON is available to physicians on request. DECADRON is a trademark of Merck & Co., Inc.

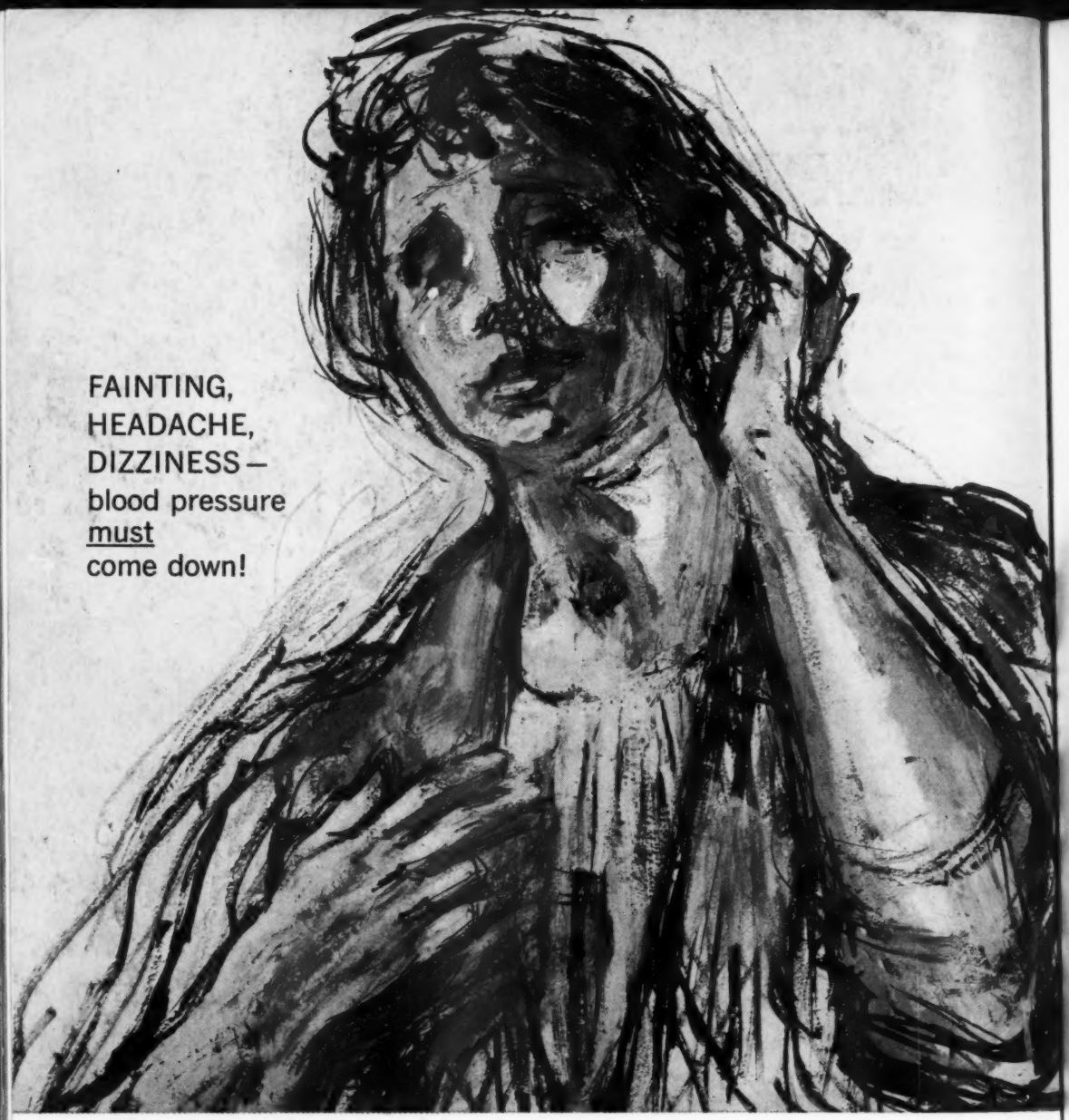
*From a clinical investigator's report to Merck Sharp & Dohme.

Decadron®

Dexamethasone

TREATS MORE PATIENTS MORE EFFECTIVELY

MERCK SHARP & DOHME • Division of Merck & Co., INC., West Point, Pa.



When blood pressure must come down

When you see such symptoms of hypertension as dizziness, headache, and fainting, your patient is a candidate for Serpasil-Apresoline. Often when single-drug therapy fails, Serpasil-Apresoline can bring blood pressure down to near-normal levels. In addition, it reduces rapid heart rate, allays anxiety.

SUPPLIED: Tablets #2 (standard-strength, scored), each containing 0.2 mg. Serpasil and 50 mg. Apresoline hydrochloride; Tablets #1 (half-strength, scored), each containing 0.1 mg. Serpasil and 25 mg. Apresoline hydrochloride.

#532

Rx New **SER-AP-ES**™ to simplify therapy of complicated hypertension

SER-AP-ES Tablets, each containing 1.0 mg. Serpasil, 25 mg. Apresoline, 15 mg. Esidrix.

SERPASIL® (reserpine CIBA) / APRESOLINE® hydrochloride (hydralazine hydrochloride CIBA) / ESIDRIX® (hydrochlorothiazide CIBA) 2/2826 HK

SERPASIL®-APRESOLINE®

CIBA

SUMMIT · NEW JERSEY